Questionnaire for Assessment of Quality of Life in Hemophilic Patients

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Abstract

Background: Hemophilia is a hereditary, persistent, hemorrhagic condition caused by a coagulation factor deficiency. Long-term spontaneous bleeding of joints and soft tissues can have a negative impact on a patient's quality of life (QoL).

Aim of the Work: This research describes the health status, health care received, and their impact on the QoL in patients with hemophilia.

Patients and Methods: This case-control study was conducted on 200 subjects: 100 patients with hemophilia, hemophilia A (HA), and hemophilia B (HB), attending outpatient clinical hematology clinics of the Internal Medicine Department, Assiut University Hospital in the period first of January 2021 up to the end of December 2021, and 100 age and sex-matched controls. All studied participants were subjected to a full history taking regarding their socio-demographic characteristics and to complete an SF-36 Qol questionnaire (Short form 36 QoL questionnaire).

Results: Hemophilia studied participants reported significantly lower QoL than control groups regarding all SF-36 items (general health, limitation of activities, physical health problems, emotional health, social activities, pain, and energy and emotions). Younger aged patients (≤ 25 years), unemployed patients, those with HA, and those with severe hemophilia had lower QoL scores compared to their counterparts.

Conclusion: The QoL of the hemophilia patients was considerably low. To overcome this issue, social support needs to be enhanced.

Keywords: Quality of Life, Hemophilia, Short form 36 Quality of life questionnaire.

1. Introduction:

Hemophilia is a hereditary condition in which patients have severe blood clotting abnormalities due to a deficiency of specific clotting factors in their blood [decrease or absence of coagulation factor VIII (HA) or factor IX (HB)]. HA accounts for roughly 85% of all instances of Hemophilia. Based on coagulation factor activity, HA and HB can be divided into three levels: mild, moderate, and severe (1).

Hemophilia affects around 400,000 persons worldwide (2). The estimated prevalence of hemophilia in Egypt is 6 per 100,000 (1), and some neighboring and regional countries per 100,000 populations were Iran 7.1, Turkey 7, Jordan 4.4, Syria

3.5, and Saudi Arabia 1.4 (3). HA is more common than HB, representing 80-

85 % of the total hemophilia population (2).

Patients typically have spontaneous bleeding of joints, muscles, and soft tissues. Approximately 80% of bleeding incidents occur in the knee, elbow, and ankle joints. Repeated joint bleeding can cause joint distortion (referred to as target joints), hemophilic arthropathy, and impairment (4).

The World Health Organization (WHO) defines QoL as "an individual's perception of their position in life in the context of the culture and value systems in which they live in relation to their goals, expectations, standards, and concerns" (5). The health-related quality of life (HRQoL) of hemophilia is much lower than that of the general population (6).

The main goal of the current study is to describe the health status, health care received, and their impact on the QoL in patients with hemophilia.

2. Patients and Methods:

This observational prospective case-control study was conducted from the first of January 2021 to the end of December 2021. The study included all hemophilic patients of different age groups, of both types (A and B), attending outpatient clinical hematology clinics of the Internal Medicine Department, Assiut University Hospital during the study period.

The study adhered to the guidelines of Assiut University's Ethical Committee (IRB No: 17100190). All participants included in this study provided informed written consent.

2.1 Eligible participants

All hemophilic diseased patients (both types A and B) of different age groups, those who received home or hospitalized treatment, patients with complications such as joint swelling, spontaneous bleeding, etc., and who accepted to participate in this study were enrolled in the current study.

The exclusion criteria were patients with other causes of bleeding tendency such as liver failure, DIC, anticoagulant drugs, etc., or diseases that affect joints such as osteoarthritis, SLE, etc., mentally disabled patients, and those who refused to participate in the study were also excluded.

2.2 Sample Size Estimation:

The sample size was calculated according to population size, anticipated frequency, level of significance, and design effect using epi info. Population size: 300.000, anticipated frequency: 50%, level of significance: 5%, and design effect: 1.0.

2.3 Methodology:

Eligible participants were subjected to the following preliminary evaluation: full history taking throughout the clinical examination, in addition to completing the following questionnaire to assess their quality of life:

- **SF-36 Qol:**

SF-36 Qol is a survey of patient health. It consists of 8 scaled scores, the weighted sums of the questions in their section.

The eight sections are: Vitality, Physical functioning, Bodily pain, General health perceptions, Physical role functioning, Emotional role functioning, Social role functioning, and Mental health. The reliability of an Arabic version of the RAND 36-Item Health Survey and its Equivalent to the US-English were validated (7), Appendix A.

2.4 Statistical Analysis:

Data were gathered and entered into the IBM SPSS (Statistical Package for Social Science, version 20). The qualitative data were presented as numbers (percentage), while quantitative data were presented as mean±standard deviation (SD) and ranges. The comparison between categorical data was done using the Chi-square test. Mann-Whitney U and Friedman tests were used to compare different QOL items in the study groups. The P-value is defined to be significant at 0.05.

3. Results

Demographic Characteristics:

The mean age of the studied cases was 26.41 ± 8.18 years (range; 18 – 72) years versus 27.10 ± 8.03 years (range; 15 – 58) years in the control group with no significant difference between them (P=0.561). Unemployed participants were significantly higher among studied hemophilia cases than their matched healthy controls (P < 0.001). Among studied hemophilia cases, 18% suffered from mild disease severity, 34% suffered from moderate disease severity, and 48% suffered from severe disease. Most hemophilia cases studied (84.0%) were HA, and 16% were HB, as shown in (**Table 1)**.

Variable name	Cases (n=100)		Controls (n=100)		P-value
Age (years)					
❖ Mean ± SD	26.41 ± 8.18		27.10 ± 8.03		0.561
❖ Median (range)	25 (18 – 72)		25.5 (15 – 58)		
❖ ≤ 25 years	52	(52.0)	50	(50.0)	0.777
❖ > 25 years	48	(48.0)	50	(50.0)	
Occupation					**0.000**
❖ Working	48	(48.0)	67	(67.0)	
❖ Student	38	(38.0)	33	(33.0)	
❖ Unemployed	14	(14.0)	0	(0.0)	
Severity					
❖ Mild	18	(18.0)			
❖ Moderate	34	(38.0)			
❖ Severe	48	(48.0)			
Type					
❖ Type A	84	(84)			
❖ Type B	16	(16.0)			

QOL between Hemophiliac and controls:

For all SF-36 items, hemophilia cases suffered significantly lower QoL than control groups (P < 0.001), as shown in (**Table 2)**.

QOL items	Cases (n=100) Mean ± SD Median (range)	Controls (n=100) Mean ± SD Median (range)	P-value
General health	55.87 ± 20.52 62.5 (0 – 100)	71.38 ± 14.47 75 (25 – 100)	**<0.001**
Limitation of activities	72.45 ± 14.38 75 (30 – 100)	97.85 ± 5.28 100 (70 – 100)	**<0.001**
Physical health problems	39.50 ± 35.03 50 (0 – 100)	96.75 ± 15.35 100 (0 – 100)	**<0.001**
Emotional health	56.00 ± 37.57 66.7 (0 – 100)	93.67 ± 18.16 100 (0 – 100)	**<0.001**
Social activities	52.75 ± 21.21 50 (0 – 100)	72.88 ± 13.77 75 (25 – 100)	**<0.001**
Pain	52.68 ± 26.50 55 (0 – 100)	83.35 ± 14.49 77.5 (45 – 100)	**<0.001**
Energy and emotions	60.42 ± 13.20 64.4 (22.2 - 84.4)	78.00 ± 6.62 77.8 (62.2 - 91.1)	**<0.001**
Mental health	47.56 ± 23.42 43.8 (0 - 93.8)	77.06 ± 11.95 75 (37.5 – 100)	**<0.001**

QOL according to age:

A statistically significant difference was observed between both studied groups regarding the limitation of activities (P=0.021), physical health problems (P=0.015), emotional health (P=0.007), energy and emotions (P=0.024), and mental health (P=0.016) which indicate lower QoL among younger aged patients (**Table 3)**.

QOL items	Age ≤ 25 years (n=52) Mean ± SD Median (range)	Age >25 years (n=48) Mean ± SD Median (range)	P-value
General health	53.13 ± 22.94 50 (0 – 100)	58.85 ± 17.29 62.5 (25 - 87.5)	0.188
Limitation of activities	69.52 ± 14.83 70 (35 – 100)	75.62 ± 13.31 80 (30 – 95)	**0.021**
Physical health problems	31.25 ± 33.16 25 (0 – 100)	48.44 ± 35.13 50 (0 – 100)	**0.015**
Emotional health	46.79 ± 35.71 66.7 (0 – 100)	65.97 ± 37.34 66.7 (0 – 100)	**0.007**
Social activities	49.04 ± 20.69 50 (0 – 87.5)	56.77 ± 21.26 62.5 (0 – 100)	0.074
Pain	48.03 ± 25.29 55 (0 – 100)	57.71 ± 27.12 67.5 (0 – 100)	0.103
Energy and emotions	57.78 ± 12.38 60 (28.9 - 75.6)	63.29 ± 13.59 66.7 (22.2 - 84.4)	**0.024**
Mental health	41.95 ± 23.66 37.5 (0 - 87.5)	53.65 ± 21.80 56.3 (12.5 - 93.7)	**0.016***

QOL according to occupational status:

Unemployed patients suffered from lower QoL regarding general health (P=0.001), limitation of activities (P < 0.000), and physical health problems (P=0.041) compared to working or student participants (**Table 4)**.

QOL items	Working (n=48) Mean ± SD Median (range)	Student (n=38) Mean ± SD Median (range)	Unemployed (n=14) Mean ± SD Median (range)	P-value
General health	55.21 ± 16.88 56.2 (12.5 - 87.5)	62.50 ± 22.88 62.5 (0 – 100)	40.18 ± 17.11 37.5 (0 - 62.5)	**<0.001**
Limitation of activities	77.50 ± 12.42 80 (30 – 100)	71.45 ± 13.20 72.5 (50 – 100)	57.86 ± 13.97 57.5 (35 – 75)	**<0.001**
Physical health problems	45.83 ± 33.95 50 (0 – 100)	38.82 ± 37.08 50 (0 – 100)	19.64 ± 26.27 0 (0 – 75)	**0.041**
Emotional health	65.28 ± 33.66 66.7 (0 – 100)	49.12 ± 40.07 66.7 (0 – 100)	42.86 ± 37.96 33.3 (0 – 100)	0.064
Social activities	55.47 ± 20.29 56 (0 – 87.5)	53.29 ± 20.69 56 (0 – 75)	41.96 ± 23.82 38 (12.5 – 100)	0.063
Pain	56.15 ± 26.96 61.2 (0 – 100)	52.43 ± 26.43 50 (0 – 100)	41.43 ± 23.53 45 (0 - 77.5)	0.173
Energy and emotions	61.25 ± 12.79 64.4 (22.2 - 84.4)	61.46 ± 13.30 65.6 (28.9 – 80)	54.76 ± 13.88 54.4 (35.6 - 82.2)	0.175
Mental health	51.95 ± 23.21 53.1 (12.5 - 93.8)	44.57 ± 23.21 46.9 (0 - 81.2)	40.63 ± 23.35 31.2 (6.2 - 81.2)	0.157

QOL according to Hemophilia type:

HA suffered from lower QoL compared to patients type HB regarding all SF-36 items (P < 0.05, for all) **(Table 5)**.

QOL items	Hemophilia type A (n=84) Mean ± SD Median (range)	Hemophilia type B (n=16) Mean ± SD Median (range)	P-value
General health	54.02 ± 21.36 50 (0 – 100)	65.63 ± 11.64 68.8 (37.5 – 75)	**0.020**
Limitation of activities	70.12 ± 14.27 70 (30 – 100)	84.69 ± 6.94 85 (65 – 95)	**<0.001**
Physical health problems	34.52 ± 33.59 25 (0 – 100)	65.63 ± 31.46 75 (0 – 100)	**0.001**
Emotional health	52.38 ± 38.82 66.7 (0 – 100)	75.00 ± 22.77 66.7 (33.3 – 100)	**0.040**
Social activities	50.00 ± 21.26 50 (0 – 100)	67.19 ± 14.34 75 (25 – 75)	**0.002**
Pain	48.90 ± 26.57 45 (0 – 100)	72.50 ± 15.14 67.5 (45 – 100)	**0.001**
Energy and emotions	58.89 ± 13.58 61.1 (22.22 - 84.4)	68.47 ± 6.90 66.7 (57.8 – 80)	**0.008**
Mental health	44.79 ± 23.68 37.5 (0 - 93.8)	62.11 ± 15.72 68.7 (31.2 – 75)	**0.007**

QOL according to disease severity:

Table 6 shows that increasing the disease severity was associated with poorer QoL among our studied cases, as we found that patients who suffered from severe disease recorded lower scores for all SF-36 items compared to patients with mild or moderate disease severity status (P < 0.05, for all).

QOL items	Mild (n=18) Mean ± SD Median (range)	Moderate (n=34) Mean ± SD Median (range)	Severe (n=48) Mean ± SD Median (range)	P-value
General health	70.83 ± 10.50 75 (50 - 87.5)	65.07 ± 15.62 62.5 (37.5 – 100)	43.75 ± 19.47 50 (0 - 87.5)	**<0.001**
Limitation of activities	85.00 ± 8.40 85 (70 – 100)	76.91 ± 8.62 80 (55 – 90)	64.58 ± 14.83 65 (30 – 100)	**<0.001**
Physical health problems	68.06 ± 29.46 75 (0 – 100)	43.38 ± 32.75 50 (0 – 100)	26.04 ± 31.77 0 (0 – 100)	**<0.001**
Emotional health	77.78 ± 34.30 100 (0 – 100)	57.84 ± 33.14 66.7 (0 – 100)	46.53 ± 38.74 66.7 (0 – 100)	**0.007***
Social activities	70.83 ± 12.13 75 (50 – 87.5)	58.82 ± 12.88 62.5 (37.5 – 75)	41.67 ± 22.38 37.5 (0 – 100)	**<0.001**
Pain	72.50 ± 28.06 77.5 (0 – 100)	59.04 ± 18.75 61.2 (0 – 100)	40.73 ± 24.95 45 (0 – 100)	**<0.001**
Energy and emotions	70.74 ± 9.09 71.1 (51.1 - 84.4)	64.71 ± 7.36 65.6 (48.9 – 80)	53.52 ± 14.02 53.3 (22.2 - 82.2)	**<0.001**
Mental health	71.88 ± 12.17 75 (50 - 93.7)	51.10 ± 17.51 50 (25 - 81.2)	35.94 ± 22.65 31.2 (0 - 87.5)	**<0.001**

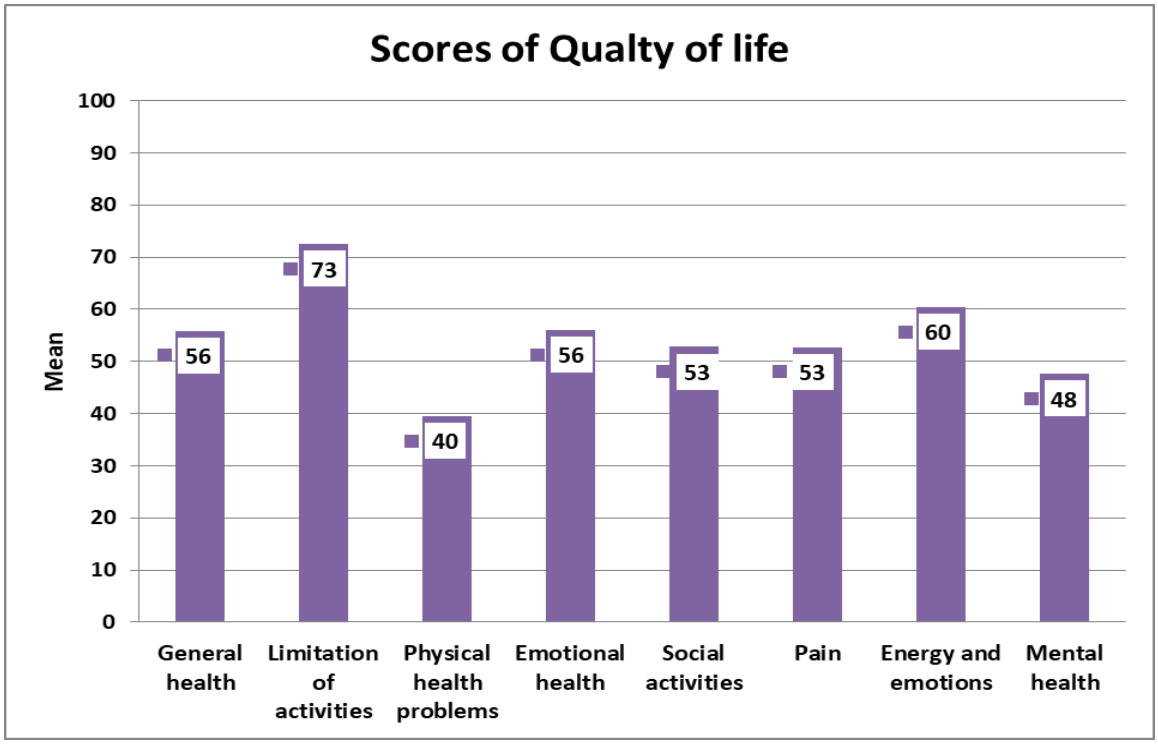

Figure 1 shows that using the Friedman test to identify the worst problem affecting the QOL among our studied cases, we observed that physical health problem was the most common problem recorded by the studied cases ($P < 0.001$).

1. Discussion

HA is the most common severe form of congenital coagulopathies. It is characterized by a deficiency of FVIII, which has serious consequences for the activation of the endogenous system of the coagulation cascade (8).

Based on the activity level of FVIII, the disease severity of HA is classified as severe: < 1%, moderate: 1-5%, mild: > 5%, and < 40% of the normal FVIII activity (9).

Consequent to the chronic nature of the disease and the complications, particularly arthritis, causing physical impairment, this disease has a severe impact on patients' QoL. Measuring the QoL makes it possible to evaluate patients' overall well-being (10).

The SF-36 has been used widely and is a helpful tool for measuring HRQoL in populations with hemophilia. However, no studies investigating HRQoL using the SF-36 in hemophilia populations report separate data for mild hemophiliacs (11).

This study aimed to describe the health status, health care received, and their impact on the QoL in patients with hemophilia. Our prospective study included hemophilic patients of different age groups, of both types (A and B), and previously diagnosed in Asyut University Hospital. Most hemophilia cases studied were HA, and 16% were HB. This was agreed with Ferreira et al. (2013), who reported that 84.6% of the participants had HA in their study (12).

The present study showed that, as regards severity, Mild was (18%), Moderate was (34%), and Severe was (48%). **Ferreira et al. (2013**) reported that 20.5% of the patients had hemophilia classified as mild, 41% as moderate, and 38.5% as severe (12).

This study for general health found that hemophiliacs suffered from significantly lower QoL compared to the control group ($P < 0.001$). According to **Walsh et al. (2008**), who aimed to measure the clinical severity of the disease, there was a significantly lower score of general health in those with hemophilia (11). Moreover, **Xu *et al.* (2017)** indicated that Hemophilia significantly negatively impacts patients' HRQoL (14).

This study for physical health problems and limitation of activities found that hemophiliacs suffered significantly lower QoL than control groups ($P < 0.001$). **Walsh et al. (2008**) found that the physical health status scales (physical functioning, physical role) had a greater than the five-point difference that is considered clinically and socially relevant (11).

Many studies reported that patients with hemophilia are less physically active than healthy controls due to fear of bleeding, insufficient recognition of the benefits of exercise, and a lack of confidence in risk assessment and management (15).

This study for emotional health found that hemophiliacs suffered from significantly lower QoL compared to control groups ($P < 0.001$). **Walsh *et al.* (2008**) showed a significantly lower score in role emotional domains in those with mild hemophilia (11).

This study for pain found that hemophiliacs suffered from significantly lower QoL compared to control groups ($P < 0.001$). Walsh et al. (2008) found that bodily pain had a greater than five-point difference, a difference that is considered clinically and socially relevant (11). In addition,

several studies have reported a high prevalence of pain in individuals with hemophilia (16).

This study found that younger patients (≤ 25 years) suffered from lower QoL regarding their general health (P=0.016). Trippoli et al. (2001) also showed that age significantly influenced the EuroQoL and the SF-36 scores (13).

Also, younger patients (≤ 25 years) suffered more from lower quality of life regarding limitation of activities (P=0.021), physical health problems (P=0.015), emotional health (P=0.007), and energy and emotions (P=0.024).

Cheung et al. (2022) show that older patients had a poorer perception of multiple aspects of their HRQoL, including perception of physical health and feelings, self-perception, and perception of the future (18).

Lower HRQoL for young in our study because, statistically, younger aged patients are the vast majority in this study, with 52 patients out of 100 ≤ 25 years old and only 26 patients ≥ 30 years old. Clinically, younger hemophilic patients have more physical demands due to work, sports, or even individual activities.

In this study, we found that unemployed patients suffered from lower QoL regarding their general health (P=0.001), limitation of activities (P < 0.00)), and physical health problems (P=0.041).

This was agreed with Niu et al. (2022), who reported that, according to this study, employment is associated with higher HRQoL of patients with Hemophilia. They found that 84.67% of the patients were not working (either on sick leave or unemployed). The impacts of the disease on work and employment are a serious concern for patients, according to the data captured by the open-ended question (1).

By comparing types of hemophilia, we found that HA suffered from lower QoL regarding all SF-36 items (P < 0.05). Recent evidence could explain this finding; there is a hint that severe HB may be clinically less severe than HA. Furthermore, in a Canadian study, it was found that patients with severe HB bled less frequently than patients with HA (19).

This study found that patients with severe disease recorded lower scores for all SF-36 items than patients with mild or moderate disease severity (P < 0.05). **Faranoush *et al*. (2017**) showed that over 50% of adult patients with severe HA in Tehran report a low to moderate level of QoL (20).

The current study revealed that using the Friedman test to identify the worst problem affecting the QOL among our studied cases; we observed that lower general health was the most common problem recorded by our studied cases (P < 0.001).

Similarly, **Baek et al. (2020)** reported that multivariate analysis revealed that consequent physical conditions affected by Hemophilia, such as Hemophilia-induced disabilities, bleeding experiences, and hemophilic arthropathy, were significantly associated with impaired HRQoL (17).

2. Conclusion

The results obtained from this study showed that the HR-QoL of the hemophilia patients was considerably low. Pain, functional impairment, and emotional health problems are present at higher levels in individuals with hemophilia. The quality of life in

patients with hemophilia was more evident at younger ages, unemployment, type A hemophilia, and severe disease.

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