Health-related quality of life in hemophilia: results of the Hemophilia-Specific Quality of Life Index (Haem-a-Qol) at a Brazilian blood center

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Background: *Studies on health-related quality of life are based on the increasingly evident need for medical care not to be limited to preventing death, but to focus instead on the value of health.*

Objective: *This study aimed to measure the health-related quality of life in hemophilia, using the Hemophilia-Specific Quality of Life (Haem-A-QoL) questionnaire and describe the socioeconomic characteristics and health conditions of these patients.*

Methods: *The Brazilian version of the Hemophilia-Specific Quality of Life questionnaire was administered to hemophiliac adults, treated in an on-demand regime at the Juiz de Fora Regional Blood Center - HEMOMINAS Foundation. The patients were interviewed about demographic and socioeconomic data and their understanding of the questionnaire. Clinical data were collected from medical records. The Mann-Whitney U test was used for statistical analysis. The level of significance was set for p-values < 0.05. Statistical analysis was performed using the Statistical Package for the Social Sciences (SPSS, version 15.0).*

Results*: Thirty-nine patients were evaluated. The mean age was 36.8 years. 84.6% had hemophilia A; 20.5% of the patients had hemophilia classified as mild, 41% as moderate and 38.5% as severe. The records of 10.5% of the patients registered seropositivity for anti-HIV and 57.9% for anti-HCV. Target joints were detected in 69.2%. The mean total Hemophilia-Specific Quality of Life score was 35.55. 'Sports and leisure' and 'Physical health' were the most impaired dimensions and the dimension 'Relationship and partners' was the least impaired. The Hemophilia-Specific Quality of Life scores showed good discriminant validity for hemophilia severity (p-value = 0.001), HIV-infection (p-value = 0.02), HCV-infection (p-value = 0.01) and the presence of target joints (p-value < 0.001).*

Conclusion*: Health-related quality of life in hemophilia, measured by the Hemophilia-Specific Quality of Life questionnaire, was influenced by the presence of arthropathy and infectious diseases transmitted by blood products. Rehabilitation measures should be encouraged in order to improve the quality of life of these patients.*

Keywords: *Hemophilia A; Hemophilia B; Musculoskeletal diseases/etiology; Joint diseases; Quality of life; Questionnaires*

Introduction

Studies on health-related quality of life (HRQoL) are based on the increasingly evident need for medical care not to be limited to preventing death, but to focus instead on the value of health[1]. HRQoL can be influenced by factors such as illness and its treatment, how the person deals with his or her problem, and access to care[2]. In the case of hemophilia, the major issues are the restrictions on physical activities, concern about bleeding that might be life-threatening, the development of arthropathy, the need for orthopedic procedures, and now, much less frequently, infectious diseases transmitted by blood or blood products[3,4].

HRQoL can be assessed using validated sensitive and specific instruments whose data are reproducible and are influenced by age and by time; these instruments should also consider the multidimensional nature of the quality of life, the physical and psychological components of the patient's perception of well-being[5]. It is also important, for the questionnaire to be useable internationally, that is, it be translated and standardized for the different cultures that the translations target[6].

As clinical evaluations may not be sufficient to adequately characterize the morbidity associated with hemophilia[7,8], the present study aimed to measure HRQoL in adults with hemophilia at the Regional Blood Center of Juiz de Fora using the Brazilian version of the Hemophilia-Specific Quality of Life (Haem-A-QoL) questionnaire. It also aimed to describe socioeconomic aspects and health conditions of these individuals in the context in which the Haem-A-QoL was assessed.

Methods

This was an observational, cross-sectional study carried out at the Regional Blood Center of Juiz de Fora (HRJF), Minas Gerais, after approval by the Ethics Research Committee of the HEMOMINAS Foundation. Informed consent was obtained from all patients involved. The inclusion criteria were to be male, 18 years or older, level of clotting factor VIII or IX less than or equal to 30%, and on hemophilia treatment in an on-demand protocol connected to the HRJF.

Participants were asked to complete the Brazilian version of the Haem-A-QoL questionnaire used with the expressed permission of the Haemo-QoL Group. They were then interviewed about the comprehensibility of the questions contained in the instrument, and about their demographic and socioeconomic data (age, self-reported skin color, education level, marital status, main occupation, personal and family income, receipt of social security benefits). Furthermore, data from medical records on hemophilia and comorbidities were collected, which included type and severity of hemophilia and the presence of clotting factor inhibitors, presence of human immunodeficiency virus antibodies (anti-HIV), Hepatitis C virus antibodies (anti-HCV) and target joints, considered by Gilbert as the initial stage of hemophilic arthropathy[9]. Data were also collected on the treatment of coagulopathies, such as: age at diagnosis, participation in the emergency home infusion program, physical activity, physiotherapy, and the use of clotting factors in the previous 12 months.

The Haem-A-QoL Questionnaire was compiled using data from focus groups of adults with hemophilia who were asked about their perceptions of their health conditions and treatment. There are 46 items divided into ten dimensions: physical health, feelings, self-perception, sports and leisure, work and school, coping, treatment, future, family planning and relationships/ partners[10]. The Haem-A-QoL was initially validated in Italy with 233 hemophilia patients. The psychometric characteristics included good reliability, high convergent validity with the SF-36 questionnaire, and high discriminant validity regarding the severity of hemophilia and the presence of infections[11]. The questionnaire was translated into Portuguese by the Mapi Research Institute and its cross-cultural validity was established with positive results from clinical reviews in 17 languages, including Portuguese[12]. The calculation of the score is performed by transforming the scores achieved in each dimension, as well as the total score, on scales ranging from zero to 100, with zero representing the best HRQoL[13].

Statistical analysis

First, the Kolmogorov-Smirnov test with Lilliefors correction was performed. This revealed the non-normality of the data. The Mann-Whitney U Test was used to compare the mean HRQoL scores. Spearman correlation analyses were conducted to evaluate the relationship between the Haem-A-QoL scores, patient age, and consumption of clotting factor concentrates in the previous 12 months. The adopted significance level was 5%. Reliability analysis was employed to determine the internal consistency with a target minimum of 0.7 for Cronbach's alpha coefficient. Statistical analysis was performed using the Statistical Package for the Social Sciences program (SPSS, version 15).

Results

Of 60 patients eligible for the study at this blood center, one was excluded before data collection began due to severe cognitive impairment resulting from central nervous system hemorrhage, 13 were not located due to outdated records and seven refused to participate in the study. Thus, 39 patients (65% of those eligible) completed the Haem-A-QoL questionnaire between May and November 2011. Participant ages ranged from 18 to 79 years (mean: 36.8 years; standard deviation: 16.8 years). The patients' demographic and socioeconomic characteristics are described in Table 1.

Table 1 - Demographic and socioeconomic characteristics of patients with hemophilia treated at the Regional Blood Center of Juiz de Fora

Variable	n	%
Age		
18 to 29 years	17	43.6
30 to 59 years	17	43.6
60 years or more	5	12.8
Self-reported skin color		
White	23	59
Brown/ bronze/ mulatto	11	28.2
Black	3	7.7
Indigenous	2	5.1
Marital status		
Single / divorced	26	66.7
Married / stable union	13	33.3
Distance between home and the blood center		
0 to 30 km	18	46.2
More than 30 km	21	53.8
Schooling		
0 to 4 years	9	23.1
5 to 8 years	9	23.1
9 to 11 years	14	35.9
12 years or more	7	17.9
Personal income in the previous month		
Up to 1 minimum wage	20	51.3
1 to 3 minimum wages	14	35.9
More than 3 minimum wages	5	12.8
Family income in the previous month		
Up to 2 minimum wages	12	30.8
2 to 5 minimum wages	15	38.5
More than 5 minimum wages	5	12.8
Unable to answer	7	17.9
Social Security benefit due to complications of hemophilia		
Yes	20	51.3
No	19	48.7
Private health plan		
Yes	15	38.5
No	24	61.5

Health conditions

Of the 39 participants, 33 had hemophilia A, and six had hemophilia B. In eight cases (20.5%) hemophilia was classified as mild (level of clotting factor VIII or IX between 5 and 30%), in 16 (41%) as moderate hemophilia (level of clotting factor VIII or IX between 1 and 5%), and in 15 cases (38.5%) as severe hemophilia (level of clotting factor VIII or IX less than 1%).

Table 2 - Mean scores and internal consistency of the dimensions that comprise the Hemophilia-Specific Quality of Life Index (Haem-A-QoL) of patients with hemophilia treated at the Regional Blood Center of Juiz de Fora

Dimension	n valid	Mean	Minimum	Maximum	Standard deviation	Cronbach's alpha coefficient
Physical health	39	43.30	0	95.00	29.58	0.72
Feeling	39	38.56	0	100.00	31.06	0.77
View of yourself	39	37.43	0	85.00	25.25	0.74
Sports and leisure	37	49.89	0	100.00	35.19	0.73
Work and school	27	29.62	0	93.75	27.44	0.83
Dealing	38	31.35	0	100.00	30.10	0.13
Treatment	39	35.47	0	78.12	23.08	0.71
Future	39	39.42	0	90.00	26.72	0.89
Family planning	32	21.41	0	100.00	33.37	0.71
Relationship/ partners	39	17.52	0	100.00	31.69	0.68
Total	39	35.33	0	79.54	20.45	0.90

Age at diagnosis ranged from 0 to 67 years, and in 58.8% of the patients the diagnosis was made after two years of life. Comorbidities reported by the patients were: asthma (10.3%), arthritis (2.6%), cancer (2.6%), heart disease (2.6%), depression (12.8%), hypertension (17.9%), chronic low back pain (15.4%), and smoking (28.9%); 66.7% considered themselves sedentary and 15.4% had a body mass index greater than 25 kg/m^2. Records of four patients (10.5%) showed seropositivity for anti-HIV and 22 (57.9%) for anti-HCV. Of 29 participants who had up-to-date test records, the presence of clotting factor inhibitor was detected in only one patient with hemophilia A (3.4%) and in no patients with hemophilia B. These results differ markedly from those released by the Ministry of Health in 2012, where 8.3% of patients with hemophilia A and 2.2% of patients with hemophilia B showed the presence of inhibitors[14].

The consumption of clotting factor VIII concentrate in the previous 12 months was quite variable. Among patients with moderate hemophilia A, it ranged from zero to 198,250 international units (IU), with an average of 51,625 IU; whereas among patients with the severe form of coagulopathy, consumption ranged from 14,750 to 174,250 IU, averaging 63,683.3 UI. Of the 31 patients with severe or moderate hemophilia, 22 (70.96%) were participating in the program for home infusions of factor concentrates in emergency situations.

The presence of target joints was detected in 69.2% of patients, i.e., the occurrence of three or more hemarthroses in the same joint in the six months preceding the study. However, only 20.5% of the study participants had received physiotherapy treatment in the previous 12 months, despite all the currently recognized benefits in the physiotherapeutic approach to rehabilitation for patients with hemophilia[15].

Health-related quality of life

The average Haem-A-QoL total score was 35.33, ranging from 0 to 79.54. The dimensions 'Sports and Leisure' and 'Physical Health' had the highest averages (49.89 and 43.30, respectively) indicating poorer quality of life, and the dimension 'Relationships and Partners' was the least impaired dimension among the participants (mean 17.52). Table 2 shows the mean scores of the Haem-A-QoL questionnaire, in total and by dimension.

The Cronbach's alpha coefficient for the instrument overall was 0.90. While in the 'Coping' dimension the alpha was 0.13, in the other dimensions it ranged from 0.68 to 0.89 in the analysis of internal consistency (Table 2).

When the Haem-A-QoL was assessed according to hemophilia severity, for patients with severe or moderate hemophilia, the dimensions 'Sports and Leisure' and 'Physical Health' were the most impaired. Yet among patients with mild hemophilia, the dimension 'Coping' showed a quite high average that was divergent from other areas (Figure 1).

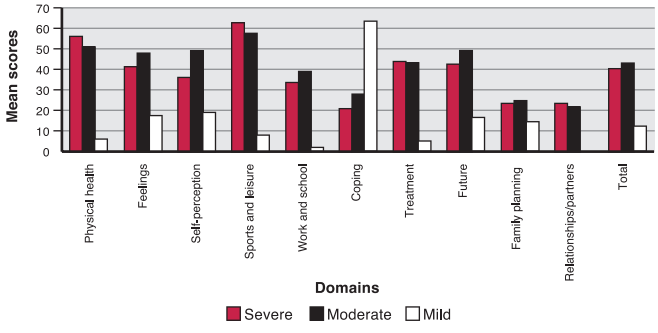

Figure 1 - Means for the Hemophilia-Specific Quality of Life (Haem-A-QoL) dimensions by hemophilia severity

The demographic, socioeconomic, and clinical characteristics that showed a statistically significant association with Haem-A-QoL are described in Table 3. The presence of target joints was strongly associated with the total score. The average was 24.56 when one or more target joints were present and 9.75 when there was no joint repeatedly affected by hemarthroses (p-value < 0.001).

The Brazilian version of the Haem-A-QoL was shown to have good discriminant validity between patients with positive and negative serology for HIV (31.25 versus 18.12; p-value = 0.025) and for anti-HCV (23.18 versus 14.44; p-value = 0.017), and between patients with mild hemophilia when compared

Table 3 - Hemophilia patient demographic, socioeconomic, and clinical variables associated with the Hemophilia-Specific Quality of Life (Haem-A-QoL) mean scores and their statistical significance

Variable	Mean	p-value
Self-reported skin color		
White	16.74	0.030
Non-white	24.69	
Personal income in the previous month		
Up to minimum wage	24.80	0.007
More than minimum wage	14.95	
Social Security benefit due to complications of hemophilia		
Yes	24.90	0.006
No	14.84	
Anti-HIV		
Positive	31.25	0.025
Negative	18.12	
Anti-HCV		
Positive	23.18	0.017
Negative	14.44	
Target joint		
Present	24.56	< 0.001
Absent	9.75	

to those with severe hemophilia (5.00 versus 15.73; p-value < 0.001) or with moderate hemophilia (5.88 versus 15.81; p-value = 0.001). No statistically significant difference was found in the Haem-A-QoL mean scores between patients with severe and moderate hemophilia (14.67 versus 17.25; p-value = 0.446).

The Haem-A-QoL total score showed a significant inverse correlation with the consumption of factor concentrates in the previous 12 months. The Spearman correlation coefficient was r = - 0.005 (p-value < 0.001). There was no correlation between patient age and the Haem-A-QoL score (r = 0.538; p-value = 0.727).

Discussion

It is recognized that many researchers have devoted their energy to the development and validation of multiple questionnaires for assessing HRQoL in hemophilia[6]. However, few results of the application of these instruments have been published. In Brazil, three studies have been conducted, two of which used generic questionnaires such as the World Health Organization Quality of Life Assessment (WHO-QOL)[16] and the SF-36[2], and only one used a specific questionnaire for patients with hemophilia[17]. As to the application of the Haem-A-QoL, only one study, conducted in Turkey in 2010, has been published in the scientific world[18].

The Brazilian version of the Haem-A-QoL proved to be a reliable instrument to assess HRQoL in adults with hemophilia. The internal consistency of the questionnaire attained a critical alpha value of 0.70. However, this value was very low in the 'Coping' dimension. The discrepant average found in this dimension may reflect ignorance of the disease and its complications by those with the mild form of hemophilia, a result of the scant guidance given to such individuals who, in general, do not exhibit spontaneous bleeding. This fact points to the need for greater precautions with this population, who may experience serious post-traumatic bleeding events, and end up being unprepared to recognize them and deal with the situation[19].

In some dimensions the HRQoL averages were higher among patients with moderate hemophilia than among those with severe hemophilia confirming the wide clinical variability among patients with moderate hemophilia[20].

In general, participants reported that the questions presented in the Haem-A-QoL were understandable and relevant in the context of hemophilia. Only one question in the 'Self-perception' dimension provoked doubts as to its interpretation. This was due to the use of words with a negative sense in both the question and the answer, which in Portuguese creates a conflict of ideas, because when one denies a denial, it seems to be invalidated.

As in the Turkish study, the dimension 'Sports and Leisure' attained the highest average, a repercussion of the high prevalence of arthropathy found in these patients. With the increased availability of clotting factor concentrates for treatment, the old practice of keeping people with hemophilia away from physical activities to prevent traumatic joint injuries needs to be forgotten. There is an increasingly well-supported tendency to encourage people with hemophilia to engage in sporting activities, not only for the physical benefits, but also as a mechanism for social inclusion[21,22].

It is noteworthy that the dimension 'Work and School' presented one of the lowest averages, which means a low loss of HRQoL in this dimension. However, 51.3% of the participants were receiving, at the time of the study, some form of social security benefit since they were considered unable to work. This discrepancy can be explained by the fact that the Haem-A-QoL questionnaire only evaluates the situation in the month preceding the study, and includes the option 'not applicable' for patients who were not involved in work or study situations during this period. This allowed a large percentage of invalid responses for this question (33.7%) thereby understating the real damage caused in the lives of these patients, most of whom are of working age.

The mean for the 'Treatment' dimension in this study (35.47) was better than that in the study conducted in Turkey (54.8), where the treatment of hemophilia is performed in general hospitals[18]. It is believed that the availability of clotting factor concentrates and the existence of specialized services for the treatment of clotting disorders are responsible for the improved quality of care provided to the patients in the present study[23].

The variability in the consumption of clotting factor concentrates was very broad, even among patients with the same severity of hemophilia. It is not known to what extent patients' difficulty of access to the blood center may have been responsible for these differences. However, in a global analysis, the average consumption of factor VIII concentrate by those with hemophilia A in the prior 12 months was 45,975.75 IU, slightly higher than the 40,000 IU recommended by the World Federation of Hemophilia to maintain moderate levels of treatment[24].

Over 70% of the patients with severe or moderate hemophilia were trained to perform home treatment, indicating good coverage by the program which periodically seeks to add new patients and families. At the time of the study, physical therapy had not yet been incorporated as routine care provided to patients with hemophilia, even though it is considered essential in the rehabilitation of these individuals[25].

Conclusion

The HRQoL in hemophilia, measured by the Haem-A-QoL instrument, was influenced by the presence of arthropathy and infectious diseases transmitted by blood products. The Brazilian version of the Haem-A-QoL proved to be a reliable instrument and exhibited good discriminant validity between clinical subgroups, but did not adequately reveal the impact of hemophilia on patients' capacity to work. As clotting factor concentrates are more widely available, physical activity, physiotherapy, and other rehabilitation measures should be encouraged in order to reduce the morbidity imposed by hemophilic arthropathy, and thus improve the health-related quality of life for people with hemophilia.

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