

Quality of life of hemophiliac

patients and satisfaction with their prophylactic treatment in Colombia

Calidad de vida de los pacientes hemofílicos y satisfacción con su tratamiento profiláctico en Colombia

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Received/Recibido: 09/25/2021 Accepted/Aceptado: 10/15/2021 Published/Publicado: 12/12/2021 DOI: <http://doi.org/10.5281/zenodo.5834683>

Abstract

Background: Hemophilia is an X-linked congenital bleeding disorder caused by a deficiency of coagulation factors. By which the therapy with recombinant and factors coagulation protein is necessary all life. This causes both physical and psychosocial changes that affect the quality of life. The objective of this research was to determine the association between quality of life, treatment satisfaction, and clinical severity of vulnerable hemophiliac patients of Cartagena-Colombia. Methods: An observational study was conducted by reviewing medical records of hemophiliacs. Quality of Life (QoL) Questionnaire Hemophilia Mexico and treatment satisfaction (TS) questionnaires were applied to patients with Hemophilia in Cartagena-Colombia. Associations between QoL and clinical severity and bivariate correlations between QoL and TS were assessed. Results: 29 hemophiliac patients between 1 and 60 years old were evaluated. 80% of patients were classified with moderate and severe hemophilia. 76% of individuals presented high QoL and 24% an average QoL; low QoL dimensions were: Knowledge about the disease, risks, physical discomforts, emotional aspects, and school or work absenteeism. TS was high, with results of 5.74 ± 0.06 (0-6 scale). There were correlations between some variables of TS with values of $R^2 > 0.1$, $p < 0.01$. Conclusions: QoL perception of patients was high despite their hemophiliac classification as moderate to severe, TS was high as well, showing a positive correlation with some QoL dimensions related directly with hemophilia and emotional aspects.

Keywords: Hemophilia A; Hemophilia B; Quality of life; Treatment satisfaction.

Resumen

Antecedentes: la hemofilia es un trastorno hemorrágico congénito ligado al cromosoma X causado por una deficiencia de factores de coagulación. Por lo que la terapia con recombinantes y factores de proteína de coagulación es necesaria durante toda la vida. Esto provoca cambios tanto físicos como psicosociales que afectan la calidad de vida. El objetivo de esta investigación fue determinar la asociación entre la calidad de vida, la satisfacción con el tratamiento y la gravedad clínica de los pacientes hemofílicos vulnerables de Cartagena-Colombia. Métodos: Se realizó un estudio observacional mediante la revisión de historias clínicas de hemofílicos. Cuestionario de Calidad de Vida (QoL) Hemofilia México y cuestionarios de satisfacción con el tratamiento (TS) se aplicaron a pacientes con Hemofilia en Cartagena-Colombia. Se evaluaron las asociaciones entre la CdV y la gravedad clínica y las correlaciones bivariadas entre la CdV y el ST. Resultados: se evaluaron 29 pacientes hemofílicos entre 1 y 60 años. El 80% de los pacientes se clasificaron con hemofilia moderada y grave. El 76% de los individuos presentó CV alta y el 24% una CV media; Las dimensiones de baja CV fueron: Conocimiento sobre la enfermedad, riesgos, malestares físicos, aspectos emocionales y absentismo escolar o laboral. TS fue alto, con resultados de $5,74 \pm 0,06$ (escala 0-6). Hubo correlaciones entre algunas variables de TS con valores de $R^2 > 0,1$, $p < 0,01$. Conclusiones: La percepción de la calidad de vida de los pacientes fue alta a pesar de su clasificación hemofílica de moderada a severa, la TS también fue alta, mostrando una correlación positiva con algunas dimensiones de la calidad de vida relacionadas directamente con la hemofilia y los aspectos emocionales.

Palabras clave: Hemofilia A; Hemofilia B; Calidad de vida; Satisfacción del tratamiento.

Introduction

Hemophilia is an X-linked congenital bleeding disorder caused by a deficiency of coagulation factor VIII (FVIII) (Hemophilia A) or coagulation factor IX (FIX) (Hemophilia B)^{1,2}. The deficiency is the result of mutations of the respective clotting factor genes, it is considered a rare disease that has a frequency of approximately one case in 10.000³. According to annual surveys from the World Federation of Hemophilia (WFH), approximately 400,000 subjects are living with hemophilia worldwide, as for Colombia, in agreement with the high-cost account report, there are 1834 Hemophiliac patients. According to this baseline, a prevalence of 0.88 /10,000 affiliated males and 0.75 /10,000 male births was defined⁴.

90% of severe HA or HB develop internal bleeding episodes into muscles or joints and usually begin at an early age^{3,5-12}. The clinical manifestation of hemophilia is hemorrhage, it normally affects joints and muscles in the lower and upper limbs, internal bleedings of digestive and urinary systems are also common, in like manner but less frequent, Central Nervous System (CNS) can be affected, this being the most severe bleeding, and the one that generates greater morbidity and mortality^{3,8,12-14}.

Diagnosis and treatment of hemophilia is a complex process, this condition goes hand in hand with both physical and psychosocial disorders that affect the Quality of Life (QoL) of the patients. According to some authors such as Sarmiento et al. (2006), the consequences and complications of hemophilia result from inappropriate management with treatment with clotting factors that lack quality, quantity, and biological safety (since they may cause inhibitors or antibodies and may not be effective). Such a situation can develop a great mental and physical burden, which can invalidate and even represent a risk of death^{15,16}. Optimal care of hemophiliac individuals, especially those with severe manifestations, promotes physical, psychosocial health and adequate control of risk factors, not only medical but environmental and so improve QoL of patients, while reducing morbidity and mortality^{14,17}.

Taking into account the absence of QoL studies of hemophiliac patients in Colombia, the impact of particular social and cultural conditions is unknown, which can be very useful to carry out more effective and pertinent interventions¹⁸. Thus the present study aimed to determine the association between QoL, Treatment Satisfaction (TS), and clinical severity of vulnerable hemophiliac patients in Cartagena city.

Methods

A descriptive epidemiological cross-sectional study was conducted to determine the association between QoL, TS, and clinical severity of vulnerable hemophiliacs of Cartagena. The sample size was 29 subjects diagnosed with hemophilia enrolled in the Colombian Hemophilia League, Cartagena Sectional. Epidemiological and clinical information was collected from the patient's medical record.

Inclusion criteria: vulnerable patients diagnosed with HA and HB (Levels of factor VIII or IX in the blood between 1 and 5% or

less than 1%) from Cartagena were included, they had to sign previous informed consent.

Exclusion criteria: patients with a bleeding disorder other than hemophilia, with psychotic disorders, and who did not agree to take part in the study.

Quality of life of patients with Hemophilia

The authors applied a specific questionnaire QoLHMex for hemophiliac patients. This instrument was developed by Dr. Osorio is made up of 63 reagents with different subscripts, for a total of 162 items, with two response options (Yes or No) and has 13 dimensions: Concentration, Self-esteem, Family Support, Activity Level, Knowledge about the Disease, Risks, Physical Disorders, Feelings about the Disease, Social Area, Emotional Area, Future, Truancy, and Joint Problems¹⁹.

Psychologist Maricela Osorio Guzmán Ph.D. provided the test, and a group of experts where Dr. Osorio Guzmán, author of questionnaire and psychology professionals validated it to Colombian patients with hemophilia^{15,20}.

Patient satisfaction with pharmacological treatment

The ESTAR satisfaction questionnaire for HIV patients that was adapted to Hemophilia was used to determine TS of patients with prophylactic replacement therapy, experts and a consistency analysis using Cronbach's Alpha validated it^{21,22}.

Statistical analysis

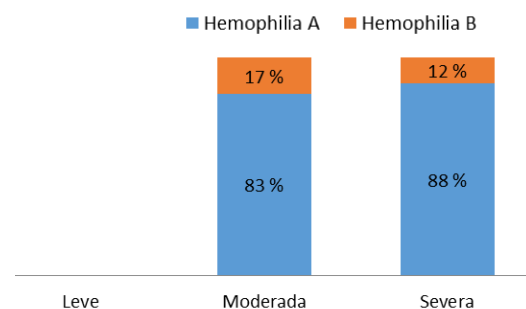
Statistical analysis included descriptive statistics for demographic, clinical, QoL, and TS data. Between QoL and TS data, Bivariate Pearson correlations were performed, accepting as P value <0.05, associations between hemophilia severity and QoL were also conducted. Statistical packages SPSS and Excel[®] were used.

Results

The study included 29 hemophiliac patients, 55.17% of them were between 1 and 20 years old, the remaining 44.83% were beyond 20. It should be noted that only 2 patients were older than 50 years. As for descriptive statistics, the mean was 16 years and mode 4 years. 86% of subjects had HA and 14% HB; 42% were diagnosed with moderate hemophilia and 58% with severe. 90% of patients received recombinant factors as prophylactic treatment and 10% received them per event.

Figure 1 shows severity, for both HA and HB, over 80% of patients presented a moderate or severe condition.

Figure 1. Clinical severity by type of hemophilia.



Quality of life

76% of patients presented a high QoL and the remaining 24% an average QoL. These outcomes are similar to those presented by Osorio et al. in 2013, where 67% of patients had an average or high QoL¹⁵.

Table 1 summarizes the main data, showing that patients presented lower QoL perception on the following dimensions: knowledge about disease (5), physical discomforts (7), emotional aspects (10), and school or work absenteeism (12).

QoL dimensions	QoL level	frequency	percentage
1) Concentration	High	24	83
	Average	5	17
	Low	0	0
(2) Self-esteem	High	23	79
	Average	6	21
	Low	0	0
(3) Family support	High	14	48
	Average	15	52
	Low	0	0
(4) Activity level	High	25	86
	Average	4	14
	Low	0	0
(5) Knowledge about the disease	High	23	79
	Average	5	17
	Low	1	3
(6) Risks	High	13	45
	Average	15	52
	Low	1	3
(7) Physical discomforts	High	6	21
	Average	22	76
	Low	1	3
(8) Feelings about the disease	High	2	7
	Average	27	93
	Low	0	0
(9) Social aspects	High	22	76
	Average	7	24
	Low	0	0
(10) Emotional aspects	High	14	48
	Average	13	45
	Low	2	7
(11) Future	High	29	100
	Average	0	0
	Low	0	0
(12) School or work absenteeism	High	5	17
	Average	21	72
	Low	3	10
(13) Joint problems	High	21	72
	Average	8	28
	Low	0	0
Total	High	22	76
	Average	7	24
	Low	0	0

Satisfaction with pharmacological treatment

Table 2 shows TS values. It can be seen that the dimension satisfaction with antihemophilic treatment was 5.6 ± 0.21 on a scale of 0 to 6, reflecting great satisfaction, with 90% of patients in six and only 0.03% in zero. The highest evaluated dimension was satisfaction with continuing treatment, which achieved an average of 5.90 ± 0.07 , reflecting satisfaction with following up on medication, in this case as in the aforementioned, 90% of patients were in six and 0.03% in zero.

The lowest dimension was satisfaction with how antihemophilic treatment adapts to your lifestyle, which obtained an average value of 5.50 ± 0.16 thus getting a ceiling effect of 90% patients in six and only 0.03% in zero.

Table 2. Condensed data on satisfaction with antihemophilic treatment, adapted from the ESTAR study

Dimensions	rank	N	Mean \pm ESM	Floor effect (% minV)	Ceiling effect (% maxV)
A. Satisfaction with antihemophilic treatment	0 a 6	29	5.60 ± 0.21	0.03	90
B. satisfaction with antihemophilic treatment efficacy	0 a 6	29	5.80 ± 0.14	0.03	90
C. Satisfaction with side effects of antihemophilics	0 a 6	29	5.90 ± 0.10	0.03	90
D. Satisfaction with treatment requirements	0 a 6	29	5.80 ± 0.10	0.03	90
E. Satisfaction with treatment comfort	0 a 6	29	5.70 ± 0.18	0.03	90
F. Satisfaction with disease knowledge	0 a 6	29	5.70 ± 0.11	0.03	90
G. Satisfaction with how antihemophilic treatment adapts to your lifestyle	0 a 6	29	5.50 ± 0.16	0.03	90
H. Satisfaction with continuing treatment	0 a 6	29	5.90 ± 0.07	0.03	90
Mean	0 a 6	29	5.70 ± 0.06		

Typified Dimensions from A to H

Associations between dimensions and questionnaires

Table 3 presents results from bivariate Pearson correlations between dimension data obtained from the QoLHMEx test. Each dimension was assigned a number from 1 to 13.

Table 3. Pearson's bivariate correlation between data from QoLHMEx test dimensions.

	(1)	(3)	(4)	(5)	(6)	(7)	(9)	(10)	(13)
(2)	0.498**			0.398**					
(5)					0.375*	-0.567**		-0.412*	
(13)						0.372*		0.412*	
QoL total		0.464*	0.469*			0.503*	0.446*	0.447*	0.666***

*. Correlation is significant at 0.05 level (bilateral). **. Correlation is significant at 0.01 level (bilateral).

Numbers are dimensions typified in QoL-MeX questionnaire (1 to 13), see Table 1.

Table 4 shows the results of Pearson's bivariate correlation between data from the TS test and some dimensions of the QoLHMex Test.

Table 4. Correlation between dimensions of QoL-MEX test vs TS test

Dimensions	(1)	(2)	(6)	(7)	(12)
D.				0.406*	
E.				-0.368*	-0.391'
F.		0.407*			
G.			-0.407*		
H.	0.486**				

** . Correlation is significant at 0.01 level (bilateral). * . La correlación es significante al nivel 0,05 (bilateral) (delete). Numbers are dimensions typified in QoL-MeX questionnaire (1 to 13), see Table 1; and letters are variables of the TS questionnaire, see Table 2.

Table 5 exhibits associations between hemophilia severity and QoL. It can be seen that 83.33% of patients with average QoL had severe hemophilia, while only 52% of patients with high QoL presented severe hemophilia.

Table 5. Relationship between clinical severity and QoL.

Clinical severity	QoL level						Total
	Low	%	Average	%	High	%	
Moderate	0	0	1	16.67	11	47.83	12
Severe	0	0	5	83.33	12	52.17	17
Total	0	0	6	20.69	23	79.31	29

Clinical severity	QoL level						Total
	Low	%	Average	%	High	%	
Moderate	0	0	1	0.08	11	91.66	12
Severe	0	0	5	29.41	12	70.58	17
Total	0	0	6	20.69	23	79.31	29

Discussion

86% of patients from this study presented HA and 14% HB, these findings are in agreement with those published by Sousa et al. in 2013²⁴ who conducted a study in the hematology center of Paraíba-Brazil. In addition, Stonebraker's study in 2011, on the prevalence of hemophilia worldwide, reported similar statistics to those found by this work. Similarly, the report situation of Hemophilia in Colombia published by the National Fund for high-cost diseases stated that HA represented 83.3% of hemophiliacs^{3,23,24}.

Regarding prophylactic treatment, the situation of Hemophilia in Colombia reported that 60.6% of patients with HA receive prophylactic treatment and 3.7% receive prophylactic treatment plus on-demand treatment, which are similar outcomes to those presented by this study. In Colombia, 55.4% of patients with HB receive prophylactic treatment, and 3.6% receive prophylactic treatment plus on-demand. Prophylactic treatment was more frequent since patients presented moderate-to-severe hemophilia²⁴.

Statement of principal findings

In relation to QoL perception, these results represent the first data in Colombia where QoL is correlated with clinical variables and TS in hemophiliacs, which constitutes the main findings of this study. Dimensions where patients presented lower QoL, were: knowledge about the disease, physical discomforts, emotional aspects, and school or work absenteeism, which is justified, considering that are patients with moderate-to-severe hemophilia who consume prophylactic treatment with factor concentrates. It is noteworthy that out of 7 patients with average QoL perception all were adults, similar results to those reported by Dekoven et al. in 2012, who through a specific questionnaire determined that adults with hemophilia present greater physical disabilities²⁵. Most studies using specific QoL questionnaires have found a clear relationship between QoL and physical disabilities such as hemarthrosis and arthropathies^{26,27}.

Overall, patients showed great satisfaction regarding their antihemophilic treatment. It should be noted that even though the used questionnaire was adapted from ARPAS I study carried out in patients with HIV²⁸, pharmacochimistry experts and psychologists validate it by verifying the objectivity of the answers. In addition, a consistency analysis with Cronbach's alpha was also conducted (0.63). Results suggest that patients embrace treatment with factor concentrates and know how important it is for their lives, which is why receiving medication on time is reflected as a satisfactory condition²².

QoLHMex test showed that the self-esteem dimension has a clear correlation with concentration and knowledge about the disease with R2 of 0.498** and 0.398**, respectively. Self-esteem and self-concept can affect memory, activity level, and concentration capacity in everyday life, including treatment dynamics, this manifests more frequently in adolescents, who according to a report by Cassis in 2007², may neglect medication and physiotherapy as they prefer to ignore the medical complications and treatment importance, this is also related to the dimension knowledge about the disease, since greater knowledge means greater self-esteem, similarly teens are often focused on the present and may not consider future consequences².

Knowledge about the disease dimension was directly correlated with risks showing an R2 = 0.375*, this suggests that patients who know more about hemophilia are more aware of both present and future risks. However, an inverse correlation was appreciated between knowledge about the disease and the dimensions of physical discomfort and emotional aspects, with R2 of -0.567** and -0.412, respectively, which is also understandable since a direct correlation was found between the dimensions of Joint Problems, physical discomfort and emotional aspects (R2 = 0.372* and 0.412* respectively), this is probably because when patients know about their disease, reduction of physical discomforts can be achieved by taking necessary precautions, and by being concerned about complications that may come from the condition, patients who know and understand the risks of hemophilia will have better chances at prevention, unlike those who are unaware. Likewise, when joint problems appear in hemophiliac patients, physical discomforts increase, and the emotional aspect is more affected, therefore it becomes important to work on self-confidence and self-knowledge.

Patients with high and average QoL were directly correlated with QoLHMex test dimension family support, activity level, physical discomforts, emotional aspects, and social aspects ($R2 = 0.464^*$; 0.469^* ; 0.503^* ; 0.446^* ; 0.447^* and 0.666^{***} , respectively). This result shows that patients QoL perception have a clear correlation to dimensions associated with the pathology, both physically and psychologically; a similar outcome was reported by Carruyo-Vizcaíno et al. in 2004³¹ where it was suggested that the mental health of individuals with hemophilia depends on the family environment since they are an important part of a comprehensive treatment, and families' attitude towards the disease can influence on clinical improvement and response to treatment²⁹.

Results from this study agree to the "Theory of reasoned action"³⁰, where authors reported the Attitude Model in Patients with Hemophilia (Modelo de Actitud en Pacientes con Hemofilia, MAPACHE, in Spanish), which stated that 72% of hemophiliacs gave greater importance to disease clinical aspects, 40% knew general aspects of the condition, and only 18% gave importance to factor deficiency, its treatments, and psychosocial aspects. MAPACHE got a slightly positive overall attitude (4.44 ± 1.12 EE) towards disease in most hemophiliacs (74.5%)²⁹.

Regarding TS vs QoLHMex questionnaire, correlation of variable Satisfaction with treatment requirements with physical discomfort dimension was 0.406^* , while the correlation between Satisfaction with treatment comfort and physical discomforts presented $R2$ of -0.368^* , thus showing direct and inverse correlations, respectively. It can be deduced that a greater comfort with treatment results in less physical discomfort, some patients stated that when treatment is more demanding, it could cause more discomfort at the time of application and because of acquisition difficulties, this was also validated by the inverse correlation obtained between the variable Satisfaction with treatment comfort and Work or school absenteeism dimension with $R2$ of -0.391 , which suggest that patients who feel more comfortable with their treatment, present less absenteeism.

The variable Satisfaction with disease knowledge presented a direct correlation with the self-esteem dimension ($R2 = 0.407^*$), thus showing that patients who are more aware of their disease have higher self-esteem, corroborating like this the direct correlation between these two dimensions of QoLHMex test. Likewise, it is important to mention that the calculated correlation between the variable's knowledge about the disease from both questionnaires recorded equal information, which constitutes reliability in applied instruments.

An inverse correlation was obtained between the variable Satisfaction with how antihemophilic treatment adapts to your lifestyle and Risks dimension, ($R2 = -0.407^*$), adaptation to treatment means fewer risks, which is logical since patients who are more adapted to their treatment have less probability of suffering unexpected medical events. Finally, Satisfaction with continuing treatment and the concentration dimension showed a direct correlation ($R2 = 0.486^{**}$), greater satisfaction with lifetime treatment contributes to a better concentration capacity and more responsiveness to environmental risk factors.

These results could be interpreted within the context of the larger literature that, despite hemophilia severity, patients have a high QoL perception, which is contradictory to what Osorio et al. reported in 2011¹⁵, where only 15.8% of patients with severe hemophilia presented high QoL perception, but it is similar to what Azjen and Fishbein reported in 1980 in their theory of reasoned action³⁰.

Strengths and limitations

One limitation of this and other studies on hemophiliac patients is that there is not enough literature that validates or generates QoL tests in Spanish. However, the main strength of our study is that emerges as a proposal for future research.

Implications for policy, practice and research

Few studies in Colombia evaluate the quality of life of hemophilia patients on prophylactic therapy with coagulation factors using a specific quality of life instrument in Spanish, so this first exploration constitutes a valuable input to be applied in health institutions that receive hemophilia patients, to implement policies and action plans aimed at improving the quality of life of patients at the regional and national level.

Conclusions

This study constitutes one of the first investigations in the Caribbean Coast of Colombia where QoL of hemophiliac patients is evaluated, therefore the impact of this disease on functionality and well-being was also assessed. We can conclude that QoL perception of patients was high despite being diagnosed as moderate-to-severe hemophiliacs, in addition, TS was also high, having a positive correlation with some QoL aspects directly related to hemophilia and emotional aspects.

Acknowledgments: Authors give special thanks to Maria Del Socorro Mendoza Perez (Vice President of the Atlantic Coast Chapter of the Colombian Hemophilia League). And to psychologist Maricela Osorio Guzmán Ph.D.

Author Contributions Antistio Alvíz Amador designed, performed, analyzed, and wrote the research paper; Antonio Diaz Caballero assisted with data analysis and writing of the paper, and Arnulfo Taron Dunoyer designed and performed of data analysis. All authors revised the manuscript and approved the ultimate version.

Compliance with ethical standards

Conflict of interest

The authors declare no conflict of interest

Ethical Considerations

The authors documented the information of hemophiliac patients following guidelines of Resolution 8430 of 1993, of the Ministry of Health of the Republic of Colombia. Helsinki Report was also accepted as an ethical benchmark in this research.

Data availability

The personal data that allowed the realization of the present study are kept in an Excel database with the information of each participating patient, these could not be available without the patient's personal information, since this violates the ethical principle of confidentiality according to the Colombian regulations Resolution 8430 of 1993.

The quality of life data generated in the present study are in an Excel database and could likewise be provided without the personal information of patients.

Short title: Quality of life of hemophiliacs

Conflict of interests: None declared by the authors.

Place of realization: University of Cartagena, Faculty of Pharmaceutical Sciences.

Acknowledgments: Authors give special thanks to Maria Del Socorro Mendoza Perez (Vice President of the Atlantic Coast Chapter of the Colombian Hemophilia League). And to psychologist Maricela Osorio Guzmán Ph.D.

Author Contributions Antistio Alvíz-Amador designed, performed, analyzed, and wrote the research paper. Antonio Diaz assisted with data analysis and writing of the paper. Arnulfo Taharon Dunoyer designed and performed data analysis. All authors revised the manuscript and approved the ultimate version.

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Abbreviations

CNS: Central Nervous System

HA: Hemophilia A

HB: Hemophilia B

QoL: Quality of life

QoLHMex: Quality of Life Questionnaire Hemophilia Mexico

TS: Treatment satisfaction

WFH: World Federation of Hemophilia

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