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Health-related quality of life among hemophilic adult patients from Iraq/Duhok

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Abstract:

BACKGROUND: A case – control study was carried out to evaluate the health-related quality of life of adult hemophilic patients.

MATERIALS AND METHODS: All registered hemophilia cases (40 cases, 36 hemophilia A and 4 hemophilia B) at Jin Blood Center in Duhok/Iraq as well as 40 normal age-matched healthy male individuals were assessed using the medical outcome study "MOS-SF (version 1.0)" so called RAND 36-item health survey 1.0, that assess eight health status scales namely: physical functioning, role-limitation due to physical health, role-limitation due to emotional problem, vitality (energy/fatigue), emotion well-being, bodily pain, social functioning, and general health.

RESULTS: The study included eight patients with mild hemophilia, 18 patients with moderate hemophilia, and 14 patients with severe hemophilia, with ages range from 17 to 57 years with the mean age of 27.85 years (±1.65). Patients with severe hemophilia were diagnosed significantly at earlier age compared with those with mild hemophilia. The study confirmed significantly reduced quality of life (QoL) in all 8 assessed areas particularly among severely affected patients with a *P* value consistently <0.001. The most affected domain was the role limitation due to physical health at 22.56% and emotional well-being at 32.71. All assessed areas were significantly preserved if early prophylaxis initiated. Other factors that were linked significantly with diminished QoL include the development of hemophilic arthropathy. The factors that did not show significant impact included positive viral hepatitis markers, presence of life-threatening bleedings, socioeconomic state, and positive family history.

CONCLUSION: Hemophilic patient displayed significant impairment of QoL, particularly after the development of arthropathy and restriction of physical activity and can be preserved with early prophylactic therapy.

Keywords:

Hemophilia, prophylaxis, quality of life, RAND 36

Introduction

Hemophilia is a sex-linked inherited genetic disorder with impaired hemostasis mostly affecting males, and results from total or partial lack of clotting factors VIII or IX.[1] It usually manifests clinically as increased bleeding tendency either spontaneously or following trauma and surgical interference. Bleeding in contrast to platelets disorders usually involves joints and muscles, which in most cases lead to chronic long-standing pain, discomforts, reduction in the range of joint movement, and ultimately progression into chronic arthritis.[2] Their consequence on joints and muscles results in disabilities and an impairment of health-related quality of life (HRQoL).[3,4]

HRQoL, as defined by the WHO, is the clear value of life features on the individual's awareness of their own location in life, in

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the background of the philosophy and worth systems in which they live, and in relation to their goals, outlooks, values and apprehensions.[5] It is a multidimensional construct concerned with the mental, emotional, social, behavioral, and physical components of well-being and function as apparent by the patients and/or observers. It is not only affected by illness and its management but also by individual features such as handling, personal insight about the primary chief causes of events in his or her life, living conditions, and socioeconomic status.[6] Studies on HRQoL are built on the progressively noticeable requirement for health maintenance that are not to be restricted in averting decease, but to emphasis instead on the benefits of healthiness.[7]

In recent years, there has been an increasing interest in assessing the consequence of hemophilia on quality of life (QoL) with a cumulative number of printed works on this topic. The assessment of HRQoL is necessary for a complete perception of the impact of a long-lasting disease on persons and to assess the influence of various management approaches.[8]

There are different studies using the disease-specific and generic HRQoL questionnaires, in particular the Medical Outcomes Study SF36, which is a famous example of a standardized QoL questionnaire that assess eight areas of life to evaluate the QoL. The outcomes of the SF36 are often compared with standard population statistics to assess the influence of a precise health disorder.[9] The current study aimed to evaluate HRQoL among adult patients with hemophilia at Duhok governorate using the SF36 questionnaire.

Materials and Methods

A case – control study carried out on all adult hemophilic patients (40 male patients, older than 16 years of age, 36 patients with hemophilia A and 4 patients with hemophilia B) registered at Jin hematology and oncology center in Duhok city/Iraq in the period between December 2020 and May 2021. It also includes 40 healthy males with comparable ages as a control group. All included patients were diagnosed with hemophilia according to the World Federation of Hemophilia guidelines (3rd edition).[10] The study was approved by the Ethical Committees of both general directorate health of Duhok and Iraqi board for medical specialties commission. Patients were acknowledged and a formal agreement was obtained from all participants at the start of the study.

Data obtained from all patients including

Residence, age of patients at the time of the study, age at first bleeding episode and diagnosis, nature and severity of hemophilia, past history of inhibitors, markers for transmitted viral infections, number of bleeding events requiring treatment in the past 3 months, life-threatening bleeding events throughout the patients' life, sites, and presence of chronic pain (pain of >3 months duration). Later on, examination done looking for the joints deformity, swelling, muscle atrophy, and limitation of movement.

Information regarding treatment included type o therapy (episodic or on demand), admission history, product used for treatment, recombinant factor VIII or cryoprecipitate. In addition to the previous information, patients further asked about education, job of the patient, marital status, and socioeconomic status.

All enrolled individuals were assessed using a reliable Arabic version of medical outcome study "MOS-SF (version 1.0)" so called RAND 36-item health survey.[11,12] This was administrated either by self-reporting or by an interview (if illiterate or unable to complete by self-administration), both Kurdish and Arabic-translated version of this questionnaire were used. This survey includes eight health status scales, namely physical functioning, role-limitation due to physical health, role-limitation due to emotional problem, vitality (energy/fatigue), emotion well-being, bodily pain, social functioning, and general health.[11] After the collection of data, scoring calculated using the scores system of the SF-36-rand questionnaire. The scores range from 0 to 100, with higher scores indicating a higher QoL, better functioning, less limitation or less pain. In step 2, the means (± standard deviations [SD]) were calculated for each the 8 domains.

Statistical and data analyses were performed using the Statistical Package for the Social Sciences software, version 22 (SPSS Inc., Chicago, IL, USA). The results were reported as mean values ± SD. The *t*-test and Pearson correlation were used as appropriate, whereas ANOVA test was used to make the comparisons between the scores among various sets of patients relating the number of complications, $P < 0.05$ was considered statistically significant.

Results

The study included all 40 male patients with hemophilia registered at Jin center and 40 age matched apparently healthy male controls. The patients' ages range from 17 to 57 years with a mean age of 27.85 years (±1.65).

From all patients, majority (18 patients (45.0%)) had moderate hemophilia followed by 14 patients (35.0%) with severe hemophilia and 4 patients (20%) with mild hemophilia. The mean age of diagnosis was

21.45 ± 6.59 months. Patients with severe hemophilia were diagnosed at mean age (12.07 ± 4.06 months), compared with those with moderate (13.02 ± 4.06 months) and mild hemophilia (56.87 ± 29.02), $P = 0.87$, <0.001, respectively.

Patients with severe hemophilia as shown in Table 1, tend to have nonsignificant higher rate of bleeding in the last 4 weeks (1.21 ± 0.26) compared to those with moderate (1.05 ± 0.20) and mild hemophilia (0.87 ± 0.89) with a $P = 0.82$ and 0.56, respectively, though the bleeding tend to be more severe in patient with severe to moderate (mainly joint bleeding) than patients with mild hemophilia (mucocutaneous bleedings). Patients with severe to moderate hemophilia develop significantly target joint at higher rate than mild hemophilic patients with a $P = 0.0432$. None of the enrolled patients had developed inhibitors.

By using the SF36 form scoring table and calculating the scores of the forty adult patients enrolled in the study, the overall mean HRQoL score was 41.9 ± 23.81, which was significantly lower than that of the enrolled matched healthy controls (84.45 ± 9.23) ($P < 0.001$). The most affected domain of the eight SF36 domains was the role limitation due to physical health at 22.56% and emotional well-being at 32.71. All of the eight domains of the SF36 form were significantly lower in adult patients as compared to the healthy controls [Table 2].

Comparing different severities, two domains including emotional well-being and social function showed significant difference in score among patient with severe hemophilia to that with mild hemophilia, with a $P = 0.021$ and 0.029, respectively [Table 3]. Despite this, no significant difference in HRQoL in all of the eight domains found between mild and moderate and also moderate with severe hemophilic patients.

Table 1: Main clinical characteristics of all patients

Parameters	Severe, *n* (%)	Moderate, *n* (%)	Mild, *n* (%)
n	14	18	8
Factor level (%)	0.77±0.06	2.26±0.19	13.11±4.65
Age	27.92±2.57	27.16±1.93	29.25±5.77
Age at diagnosis	12.07±4.06	13.02±4.06	13.11±4.65
Bleeding in last 4 weeks	1.21±0.26	1.05±0.20	0.87±0.89
Target joint	13 (92.86)	18 (100)	5 (62.5)
Chronic pain	7 (50)	5 (13.88)	1 (12.5)
Joint impairment	8 (57.1)	7 (38.88)	2 (25.0)
Poor socioeconomic state	5 (35.7)	9 (50)	1 (12.5)
Family history	11 (78.57)	15 (83.3)	7 (87.5)
Viral hepatitis			
B	1	1	0
C	2	1	1
B + C	0	2	0
Mode of therapy			
Episodic	14	16	8
Prophylaxis	0	2	0

No significant difference in HRQoL in all the eight domains in relation to the socioeconomic status of the hemophilic patients, while significant lower scores of hemophilic HRQoL in four domains (energy and fatigue, social functioning, general health, and emotional well-being) in patients having more than one bleed per month than those having no bleeds. Patients having chronic pain have significantly lower scores in two domains (role of physical function and general health), $P < 0.05$, Table 4.

Another significant difference seen in one domain only (role of emotional) in relation to family history as patients with positive family history had significantly lower score in comparison to those with negative family history. Furthermore, significant lower result in patients having episodic treatment in all eight domains of HRQoL in comparison to patients on prophylaxis [Table 4].

Although the overall mean HRQoL was higher in hemophilic patients having life-threatening bleeding and viral hepatitis, none of them were significantly different in all of the eight domains. While there was significant difference in all of the eight domains of HRQoL in regards of joint impairment having $P < 0.05$ [Table 5].

Discussion

Hemophilia is worldwide genetic disease affecting one in every 10000 new-born and manifests as increased bleeding tendency, particularly into joints and muscles.[13] It is a chronic disease that can have a burden on the QoL of affected individuals and despite the widespread epidemiology of the disease, limited data are available particularly on the HQoL of affected individuals in the Middle East, thus the current study initiated to tackle such paucity of data in the Iraq/Duhok.

Numerous studies established previously connect several factors to the clinical behavior of the disease including severity of the disease as mild cases demonstrated lower impact of the disease on the emotional and social parameters of HRQoL of enrolled patients.[14] Fortunately, one factor documented to be negatively linked with the QoL in hemophilic patients and that have psychosocial effect on their families and caregivers, inhibitor development was not detected among our patients.[15] This, in contrast to the global data on inhibitor development with accumulative incidence of FVIII inhibitors reaching to approximately 25% (0%–52%) in patients with severe hemophilia A, and previous data from Iraq with an incidence of 11.6%–22.2%,[16-19] may reflect the targeted studied population (adults) with

Table 2: Health-related quality of life (short form 36) score (%) comparison between adult patients with hemophilia and healthy controls

Category	HRQoL (mean±SD)									
	Age	Physical function	Role of physical	Role of emotional	Energy fatigue	Social function	Pain	General health	Emotional well being	Overall mean
Control	28±8.30	92.19±8.29	92.07±13.03	92.66±13.99	72.31±9.62	88.23±12.79	84.26±15.31	81.34±10.66	72.56±11.04	84.45±9.23
Patients	27.6±10.4	47.80±25.83	22.56±37.41	48.46±20.73	46.21±19.80	49.08±22.25	46.28±24.82	42.58±18.92	32.71±44.14	41.96±23.81
P	0.86	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001

SD=Standard deviation, HRQoL=Health-related quality of life

lower incidence of inhibitors, genetic background, racial factors, or small number of studied patients.[20,21]

All parameters of HRQoL particularly of role of physical and emotional well-being were lower than that of normal individuals and lower than that reported from hemophilic patients from European countries, but comparable to those reported from Brazilian hemophilic patients.[22,23] With the early diagnosis, education of the families' members particularly of those with new mutation "as 7/40 (17.5%) patients do not have family history," and early initiation of prophylaxis decreases the episodes of bleeding and hence the establishment of hemophilic joint diseases, possibly severe discomfort, pain and incapacity as a result, and enhances the patients' HRQoL. Our findings of relatively small number of patients (2 cases from 40), were comparable to that reported from a study conducted from Italy on elderly patients aged > 65 years with severe hemophilia, the vast majority of patients who failed to receive prophylactic therapy, showed severe reductions in HRQoL, with a negative impact on the emotional and social comfort as compared to healthy controls and also inferior orthopedic standing which negatively associated with HRQoL.[24]

The major complication revealed to have impact on all eight areas of QoL in the present study was the development of the hemophilic arthropathy as in patients with hemophilia, the main problem is the limitations on physical activities, fear of hemorrhage that could be serious and life-threatening, the establishment of arthropathy, the necessity for orthopedic interferences, and currently less likely complication, infections transmitted by blood and blood products.[25]

Limitation

Small numbers of patients included as all registered cases enrolled. Furthermore, limited number of patients on prophylactic therapy in comparison to those with on demand therapy due to unavailability of the factor VIII for prophylactic therapy.

Conclusion

Patients of hemophilia have impaired QoL, particularly after the development of arthropathy and restriction of physical activity and can be improved with prophylactic therapy.

Ethical approval

The study was approved by the ethical committee of both general directorate health of Duhok and Iraqi board for medical specialties commission. Verbal informed consent was obtained after the study was explained to the patients.

Table 3: Health-related quality of life of adult hemophilic patient short form 36 score (%) in relation to the severity of factor deficiency

Category	HRQoL (mean±SD)								
	Physical function	Limitation physical	Pain	General health	Emotional	Social	Energy	Limitation emotional	Mean±SD
Mild (8 patients) versus moderate (18 patients)									
Mild	58.75±30.09	40.62±44.19	57.50±33.67	55.13±30.80	64.38±26.23	64.06±26.25	60.0±26.05	43.75±47.72	55.52±31.48
Moderate	53.42±23.51	27.63±42.40	50.52±21.67	41.57±13.23	47.73±17.63	50±18.16	45±17.95	29.81±42.87	43.21±22.42
P	0.862	0.668	0.765	0.194	0.117	0.261	0.158	0.744	0.339
Mild (8 patients) versus severe (14 patients)									
Mild	58.75±30.09	40.62±44.19	57.50±33.67	55.13±30.80	64.38±26.23	64.06±26.25	60.0±26.05	43.75±47.72	55.52±31.48
Severe	33.93±21.77	5.36±14.47	34.11±19.28	36.79±14.62	40.36±17.15	39.29±21.29	40±15.32	30.36±46.18	32.52±17.40
P	0.067	0.080	0.078	0.072	0.021	0.029	0.056	0.781	0.085
Moderate (18 patients) versus severe (14 patients)									
Moderate	53.42±23.51	27.63±42.40	50.52±21.67	41.57±13.23	47.73±17.63	50±18.16	45±17.95	29.81±42.87	43.21±22.42
Severe	33.93±21.77	5.36±14.47	34.11±19.28	36.79±14.62	40.36±17.15	39.29±21.29	40±15.32	30.36±46.18	32.52±17.40
P	0.071	0.195	0.133	0.737	0.531	0.325	0.735	0.999	0.133

SD=Standard deviation, HRQoL=Health-related quality of life

Table 4: Health-related quality of life of adult hemophilic patients and its relation to some clinical and socioeconomic parameters

Category	HRQoL (mean±SD)								
	Physical function	Role of physical	Role of emotional	Energy fatigue	Social function	Pain	General health	Emotional well being	Overall mean
Number of bleeds									
No bleeds (8 patients)	57.78±29.27	38.89±46.96	55.54±47.14	61.67±23.98	63.89±28.25	58.33±30.79	58.89±26.55	63.89±23.67	57.36±30.40
≥1 bleed (32 patients)	45.00±24.56	17.97±33.74	26.30±41.80	41.88±16.40	44.92±18.74	42.89±22.28	38.00±13.46	44.13±17.93	37.63±20.12
P	0.194	0.239	0.079	0.006	0.022	0.100	0.048	0.010	0.96
Chronic pain									
Absent (27 patients)	52.68±26.09	31.25±41.74	36.01±33.90	48.93±21.49	52.68±23.66	49.37±27.72	46.64±20.33	51.96±21.48	46.19±25.79
Present (13 patients)	37.31±22.78	3.85±13.87	25.64±43.62	40.38±14.64	41.35±17.22	39.61±15.97	33.85±11.93	40.92±17.45	32.86±16.20
P	0.076	0.003	0.491	0.146	0.131	0.163	0.042	0.114	0.52
Family history									
Absent (7 patients)	55.63±18.98	40.63±46.17	66.66±47.14	50.00±22.68	62.50±18.90	60.00±22.20	51.25±14.08	53.50±23.12	55.02±24.12
Present (33 patients)	45.91±27.14	18.18±34.39	24.49±39.90	45.30±19.32	45.83±22.02	42.95±24.58	40.48±19.52	47.24±20.31	38.80±22.99
P	0.364	0.130	0.013	0.554	0.056	0.081	0.151	0.451	0.084
Socioeconomical status									
Poor (15 patients)	43.00±26.58	25.00±37.80	29.99±40.80	41.67±18.09	45.83±22.49	40.17±21.35	41.00±11.37	43.80±20.52	38.81±22.70
Intermediate or good (25 patients)	50.58±25.51	21.15±37.88	34.29±46.68	48.85±20.60	50.96±22.34	49.81±26.37	43.50±22.32	51.15±20.77	43.79±24.69
P	0.372	0.756	0.768	0.269	0.484	0.236	0.638	0.279	0.526
Type of treatment									
Prophylaxis (2 patients)	95.00±0.00	100.00±0.00	100.00±0.00	95.00±0.00	100.00±0.00	100.0±0.00	97.50±3.54	97.50±3.54	98.12±0.00
On demand (38 patients)	45.38±24.07	18.59±33.79	29.27±42.44	43.72±16.77	46.47±19.44	43.53±22.11	39.77±14.48	45.95±17.86	39.08±20.55
P	0.006	0.002	0.000	0.000	0.000	0.001	0.000	0.000	0.000

SD=Standard deviation, HRQoL=Health-related quality of life

Table 5: Health-related quality of life of adult hemophilic patients and its relation to some common complication

Category	HRQoL (mean±SD)								
	Physical function	Role of physical	Role of emotional	Energy fatigue	Social function	Pain	General health	Emotional well being	Overall mean
Joint impairment									
Absent (23 patients)	55.63±26.92	34.38±44.12	44.09±47.93	53.13±21.66	56.77±21.80	54.27±27.49	47.54±20.96	57.58±20.96	50.42±25.83
Present (17 patients)	36.76±20.15	5.88±14.06	16.66±33.20	36.47±11.56	38.23±18.47	35.00±14.95	35.59±13.21	35.59±14.43	30.02±14.13
P	0.019	0.006	0.037	0.003	0.007	0.007	0.045	0.000	0.003
Life threatening bleeds									
Absent (38 patients)	46.79±25.33	21.15±36.06	31.83±43.63	45.64±18.22	48.40±20.91	45.51±23.61	41.69±17.19	47.77±19.14	41.10±22.36
Present (2 patients)	67.50±38.89	50.00±70.71	50.00±70.71	57.50±53.03	62.50±53.03	61.25±54.80	60.00±49.50	62.00±53.74	58.84±55.55
P	0.274	0.293	0.577	0.805	0.771	0.389	0.693	0.772	0.730
Hepatitis									
Negative (32 patients)	45.45±22.96	16.67±31.66	26.51±41.16	43.48±18.31	46.21±20.13	44.01±24.00	40.48±16.48	46.42±20.05	38.66±21.11
Positive (8 patients)	57.50±35.66	46.88±50.77	58.32±49.60	57.50±22.99	60.94±27.90	55.62±27.64	51.25±26.42	56.88±22.76	55.61±30.64
P	0.388	0.145	0.067	0.142	0.093	0.240	0.151	0.205	0.070

SD=Standard deviation, HRQoL=Health-related quality of life

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Conflicts of interest
There are no conflicts of interest.

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