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Quality of life and clinical assessment of joint health in children with hemophilic arthropathy

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Abstract

Background: Hemophilic arthropathy results in pain, deformity, and disability with severe impairments, activity limitation, and thus productivity loss. Also patterns of treatment interfere with patients' life, so the quality of life should be assessed when evaluating treatment. The aim of this work was to assess the quality of life of children with hemophilic arthropathy and its relation to clinical joint health.

Results: The study was carried out on fifty boys with hemophilic arthropathy. All patients were subjected to thorough local clinical assessment of the most affected and/or target joint using Hemophilia Joint Health Score (HJHS 2.1) and assessment of quality of life using Haemo quality of life (Haemo-Qol) questionnaire children and parent versions. Among the fifty hemophilic patients, 36 (72%) patients were hemophilia A and 14 (28 %) patients were hemophilia B. The age at first hemarthrosis ranged from 1 to 8 years with a mean of 2.40±1.78. While the number of joints affected in the studied patients ranged from 2 to 13 joints with a mean of 7±3.25. As regards the severity, 23 patients (46%) had severe, and 27 (54%) had moderate hemophilia. Forty four (88%) patients had different degrees of anemia. There was significant correlation between child Haemo-QoL with degree of anemia ($r = 0.291$, $P = 0.040$), mainly with view and school dimensions. There were significant correlations between child and parent Haemo-QoL and HJHS with each of the following: factor activity level, duration of the disease, duration of joint disease, number of bleeding attacks last year, and number of joints affected. Synovectomy was done for 5 (10%) patients. The total child Haemo-QoL score was statistically significantly lower after the intervention (P=0.043), with a significant improvement in physical health, feeling, view, family, school and sports, treatment, and dealing dimensions. In the current study, there were significant positive correlations between child and parent Haemo-QoL and HJHS scores.

Conclusions: The quality of life in patients with hemophilic arthropathy was influenced by the joint health, factor activity level, disease duration, number of bleeding attacks, number of joints affected (during life), duration of joint disease, and presence of hepatitis C virus.

Keywords: Hemophilia Joint Health Score, Health-related quality of life in hemophilia Haemo quality of life, Hemophilic arthropathy

Background

Hemophilic arthropathy is a disabling immune-mediated arthritis caused by chronic and recurrent exposure of the synovium and articular cartilage to metabolized blood products. The presence of the iron-rich breakdown product hemosiderin is thought to promote the production of pro-inflammatory cytokines [1].

Arthropathy is a frequent and serious complication of repeated joint bleeding in patients with hemophilia, resulting in pain, deformity, and disability. Despite advances in treatment and the delivery of comprehensive care at dedicated centers, joint bleeding and arthropathy remain among the most common complications of hemophilia and are major concerns of clinicians and patients [2].

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Assessment of joint status in children with hemophilia using the Hemophilia Joint Health Score (HJHS) is preferred above the formerly used orthopedic joint score designed by Gilbert [3].

The HJHS is a scoring instrument that was developed by the International Prophylaxis Study Group (IPSG) physiotherapy expert working group. It is a useful tool for identifying and tracking changes in joint health in hemophilia with respect to therapy or disease progression. It is also a useful tool for the detection of early joint damage [3, 4].

Assessing the outcome of treatment is an essential component of evaluating practice. Within medical research, the need to assess patient-based outcomes has increased during recent years. One important outcome for the evaluation of hemophilia care is health-related quality of life (HRQoL) [5].

The Haemo quality of life (Haemo-QoL) was a disease-specific QoL questionnaire designed to assess the quality of life of hemophilia children and their parents. It was recently field-tested in six European countries (Germany, Italy, France, Spain, Netherlands, and the UK) involving 339 children from 20 centers [6], and the structure of the questionnaire showed acceptable psychometric properties [6, 7].

The aim of this work was to assess the quality of life of children with hemophilic arthropathy and its relation to clinical joint health.

Methods

The study was descriptive cross-sectional carried out on fifty boys aged 4 to 16 years, with hemophilic arthropathy [8]. They were selected from those attending the outpatient Hematology Clinic of Alexandria University Children's Hospital at El shatby. We excluded children with co-morbid illness such as juvenile idiopathic arthritis, muscular dystrophy, and neuropathic arthropathy that cause osteoarticular findings that may obscure or confound the hemophilia-based joint findings. Also, non-cooperative patients or patients with acute bleeding within 2 weeks prior to testing were excluded from the study.

Parents of all children included in the study were informed about the nature and details of the work, and a written consent was taken from them. The study was approved by the Local Ethics Committee, Faculty of Medicine, Alexandria University.

All patients were subjected to:

1-Thorough history taking consisting of the following:

a-Personal data including age, residence, family size, sequence of the child in the family, father and mother education, and school grade.

b-Bleeding history including hemophilia type, factor activity level, age at first bleeding (months), disease duration, age at first hemarthrosis (years), number of bleeding attacks (last year), number of joints affected (during life), duration of joint disease (years) (age of the patient on examination—age of first hemarthrosis), and type and mode of treatment.

2-Thorough clinical assessment for presence of other sites of bleeding than joints and local assessment of the most affected and/or target joint using hemophilia joint health score (HJHS 2.1) [9–12].

The target joint was defined as the joint in which recurrent bleeding has occurred four or more times in the past 6 months [12].

The HJHS version 2.1 is an eight-item tool developed to assess joint impairment of the six key index joints (elbows, knees, and ankles) in hemophilia. These items include swelling, duration of swelling, muscle atrophy, crepitus on motion, flexion and extension loss, joint pain on motion, and strength. In addition, the HJHS version 2.1 incorporates a global gait analysis as a ninth item. The maximum disease score for each joint is 20, with a possible total score of 120, plus a maximum of four for global gait. The global gait score assesses walking, hopping, running, and stair skills with scores of 0–4. In HJHS 2.1, higher score means worse joint health.

3-Assessment of the quality of life using The Haemo-QoL questionnaires: [7, 13–15]

The Haemo-QoL questionnaires were designed to assess HRQoL in patients with hemophilia. Two versions of Haemo-QoL, one completed by parents and one by children, are available for each of the following age groups: 4–7 years (21 items covering 8 dimensions), 8–12 years (64 items covering 10 dimensions), and 13–16 years (77 items covering 12 dimensions). All versions are self-administered except the version for children aged 4–7 years.

For all questionnaires in the Haemo-QoL family, scoring rules have been defined to specify how dimension scores and a total score summarizing HRQoL of patients can be calculated. Scales were transformed from 0 to 100 in order to be comparable; lower scores indicate better HRQoL and higher scores indicate a high impairment in QoL.

4-Laboratory assessment:

a-Complete blood count was done for all patients. Hemoglobin level was used to classify the degree of anemia if present to mild, moderate, and severe [16].

b- Test for detection of hepatitis C virus.

Statistical analysis of the data [17]

Data were fed to the computer and analyzed using IBM SPSS software package version 20.0. (Armonk, NY: IBM

Corp). Qualitative data were described using number and percent. The Kolmogorov-Smirnov test was used to verify the normality of distribution. Quantitative data were described using range (minimum and maximum), mean, standard deviation, and median. Significance of the obtained results was judged at the 5% level.

Results

The age of the studied patients ranged from 4 to 16 years with a mean of 9.64 ± 3.35 years. As regards residence, 28 (56%) of the studied patients live in rural areas while 22 (44%) live in urban areas. Family size of the studied patients ranged from 3 to 8 people with a mean of 4.86 ±1.25 people. The sequence of the patient in the family was as follows; he was the first child in 15 (30%) families, the second in 24 (48%), the third in 8 (16%), and above that in 3 (6%) families. Regarding father education of the studied patients, 31 (62%) were illiterate and 19 (38%) were educated. As regards mother education of the studied patients, 29 (58%) were illiterate and 21 (42%) were educated. According to the school grade, 8 (16%) patients were in kindergarten, 29 (58%) patients were at primary school, 8 (16%) patients were at preparatory school, and 5(10%) patients were at secondary school.

Distribution of hemophilic patients according to bleeding history was presented in (Table 1). All hemophilic patients were receiving on demand therapy, 4 patients (8.0%) received plasma transfusion, 2 patients (4.0%) received both plasma and cryoprecipitate, 25 patients (50.0%) received either plasma or factor, and 19 (38.0%) patient received plasma, factor, and cryoprecipitate.

The most common target joint was the knee (72%), followed by the ankle (10%), and then the elbow (4%) (Figs. 1 and 2).

Data of assessment of target joints by HJHS score were presented in (Table 2).

Hemophilia joint health score (HJHS)

As regards the child Haemo-QoL score dimensions, view and sports and school were the only two dimensions that showed statistically significant difference among the three age groups with *P* value of 0.001 and 0.005, respectively (Table 3).

With respect to parent Haemo-QoL score, physical health and view were the only two dimensions that showed statistically significant difference among the three age groups with *P* value 0.004 and ˂0.001, respectively (Table 4).

A significant correlation between child and parent Haemo-QoL and HJHS with each of the following: severity of hemophilia (factor activity level), duration of the hemophilia, number of bleeding attacks last year, duration of joint disease, and number of affected joints (Table 5).

Table 1 Distribution of hemophilic patients according to bleeding history

Bleeding history	
Type of hemophilia (number of patients)	
Hemophilia A	36 (72%)
Hemophilia B	14 (28%)
Factor activity level (number of patients)	
Moderate (1–5%)	27 (54.0%)
Severe(<1%)	23 (46.0%)
Age at the first bleeding (month)	
Min-max	1–72
Mean± SD	11.00±15.83
Disease duration (year)	
Min-max	1–16
Mean± SD	9.04±3.53
Age at first hemarthrosis (year)	
Min-max	1–8
Mean± SD	2.40±1.78
Duration of joint disease (year)	
Min-max	1–15
Mean± SD	7.34±3.51
Number of bleeding attacks last year	
Min-max	4–30
Mean± SD	13.10±5.58
Number of joints affected	
Min-max	2–13
Mean± SD	7.00±3.25

There was no statistical significant differences between child and parent Haemo-QoL score among the different age groups.

No statistical significant relations were found between child and parent Haemo-QoL with residency, sequence of the child in the family, and father education.

Only, there was significant relation between child and parent Haemo-QoL with mother education with *P* value of 0.002 and 0.011, respectively.

On the other hand, there was a statistical significant difference between HJHS (*F* test=9.843, *P* value <0.001) among the different age groups with an increase in the scores as the age advances (Table 6).

As regards anemia, 44 (88%) patients had different degrees of anemia. There was a significant correlation between child Haemo-QoL with degree of anemia ($r = 0.291$, $P = 0.040$), mainly with view (*P* 0.001) and school (*P* 0.002) dimensions. While there was no statistical significant correlations with parent Haemo-QoL (*P* 0.106).

Hepatitis C virus infection was recorded in 4 patients, and a significant relation was found between it and child

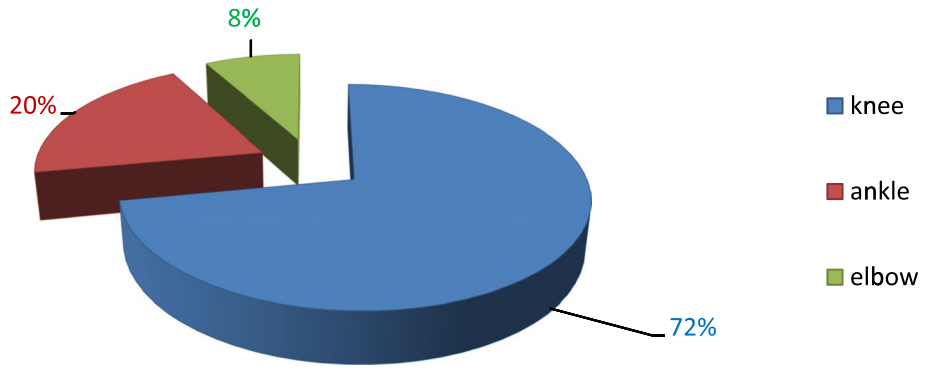

Fig. 1 Distribution of hemophilic patients according to the most affected and/or the target joint

and parent Haemo-QoL with *P* value 0.024 and 0.040, respectively.

Only five (10%) of the studied patients did synovectomy. The total child Haemo-QoL score was statistically significantly lower after the intervention (*P*=0.043), with a significant improvement in physical health, feeling, view, family, school and sports, treatment, and dealing dimensions.

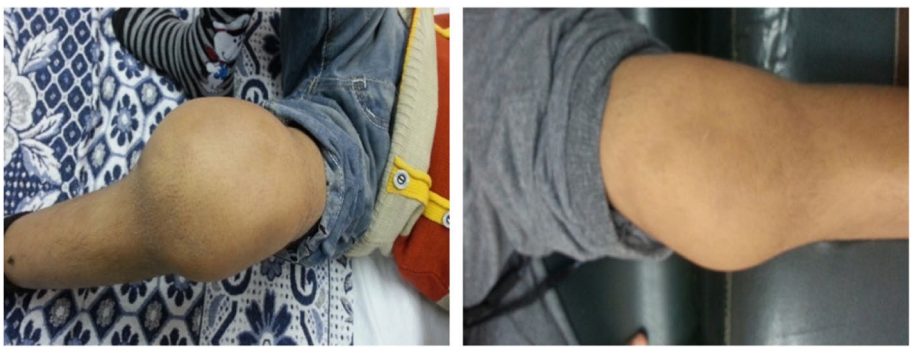

Fig. 2 Patient with hemophilic knee joint

In the current study, there were significant positive correlations between total score of child and parent Haemo-QoLwith total HJHS scores ($r = 0.620$, $P<0.001$ for child and $r = 0.630$, $P<0.001$ for parents).

Discussion

One important outcome for the evaluation of hemophilia care is health-related quality of life (HRQoL) [18]. It was defined as the subjective assessment of the impact of disease and treatment across the physical, psychological, social, and somatic domains of functioning and wellbeing [9].

Regarding child haemoQol, group one children had least impairment in the dimension of view with statistically significant difference among the three age groups. This may be due to the reason that preschoolers are naturally curious about their surroundings and are just beginning to experience day to day activities and still have a little knowledge about the disease and its complications. Preschoolers in general may not be able to understand the concept of cause and effect, which is learned during the school.

Group two children had most impairment in the dimension of sports and school with statistically significant difference among the three age groups. Overprotectiveness may be the reason as the teachers and parents may prevent them from participating in school activities to avoid trauma and hemarthrosis. This may be explained as, at the age of six, children change their stage of education from kindergarten to the primary stage where they acquire new skills and face a broader area of practice but because of their disease they find it difficult to acclimate. At an older age from 13 to 16 years (group three), children may have been adapted with their illness making their score better than group two.

Table 2 Distribution of hemophilic patients according to items of HJHS score

Items of HJHS	*n*=50	%
Swelling		
No	2	4
Mild	10	20
Moderate	26	52
Severe	12	24
Duration of swelling		
No swelling or <6 months	20	40
≥6 months	30	60
Muscle atrophy		
None	13	26
Mild	24	48
Severe	13	26
Crepitus of motion		
None	22	44
Mild	20	40
Severe	8	16
Flexion loss		
<5	5	10
5–10	16	32
11–20	18	36
>20	11	22
Extension loss		
<5	8	16
5–10	17	34
11–20	17	34
>20	8	16
Joint pain		
No pain through active range of motion	16	32
No pain through active range of motion, only pain with gentle overpressure or palpation	13	26
Pain through active range of motion	21	42
Strength		
Holds test position against gravity with maximum resistance (grade 5)	8	16
Holds test position against gravity with moderate resistance (but breaks with maximal resistance) (grade 4)	14	28
Holds test position with minimal resistance (grade 3+) Or holds test position against gravity (grade 3)	20	40
Able to partially complete range of motion against gravity (grade 3−/2+) Or able to move through range of motion gravity eliminated (grade 2) Or through partial range of motion gravity eliminated (grade 2) trace (grade 1) or no muscle contraction (grade 0)	8 0	16 0
Global gait (walking, stairs, running, and hopping on one leg)		
All skills are within normal limits	7	15.2
One skill is not within normal limits	3	6.5
Two skills are not within normal limits	15	32.6
Three skills are not within normal limits	11	23.9
No skill are within normal limits	10	21.7

Table 3 Comparison between the child Haemo-QoL score dimensions among the different age groups

Dimensions	Child			Test of sig	*P*
	Group I (4–7 years)	Group II (8–12 years)	Group III (13–16 years)		
Physical health					
Min-max	25-100	46.4–92.60	53.50–92.80	$^{KW}\chi^2$=3.713	0.156
Mean ±SD	62.50±24.02	70.93±11.94	76.43±12.69		
Feeling					
Min-max	33.3-83.3	10.70–82.10	43.70–90.60	$^{KW}\chi^2$=1.130	0.568
Mean ±SD	57.11±19.29	60.81±15.84	66.88±15.46		
View					
Min-max	0-75	11.10–83.20	25.0–92.5	$^{KW}\chi^2$=15.084*	0.001*
Mean ±SD	39.28±21.29	60.95±18.16	69.58±20.25		
Treatment					
Min-max	25-100	46.4–89.2	18.7–93.7	$^{KW}\chi^2$=0.123	0.941
Mean ±SD	64.28±25.41	63.95±13.05	59.07±24.56		
Sports and school					
Min-max	16.6-83.3	56.2–93.7	25.0–88.8	$^{KW}\chi^2$=10.515*	0.005*
Mean ±SD	58.29±19.33	75.23±9.26	72.86±16.31		
Other persons					
Min-max	25-75	0–70.8	25.0–83.3	$^{KW}\chi^2$=5.047	0.080
Mean ±SD	42.86±20.64	49.27±18.17	60.73±17.89		
Friends					
Min-max	0-100	18.70–81.70	18.70–81.20	$^{KW}\chi^2$=4.497	0.106
Mean ±SD	50.00±27.73	45.29±15.67	60.39±22.67		
Family					
Min-max	37.5-87.5	35–90	56.2–87.5	$^{KW}\chi^2$=3.411	0.182
Mean ±SD	69.64±11.72	67.71±12.68	74.77±9.28		
Dealing					
Min-max		10.70–78.50	25–75	*Z*=0.304	0.761
Mean ±SD		56.21±14.51	57.70±13.85		
Perceived support					
Min-max		25–75	37.50–87.50	*Z*=1.545	0.122
Mean ±SD		51.81±11.28	61.44±16.83		
Future					
Min-max			25–100		
Mean ±SD			63.53±24.39		
Relationships					
Min-max			25–87.50		
Mean ±SD			65.63±24.49		

Haemo-QoL Haemo quality of life

$^{KW}\chi^2$ chi-square for Kruskal-Wallis test, *Z*: for Mann-Whitney test

*Statistically significant at $P \leq 0.05$

Holmbeck et al. [19] in their study of 68 families with a chronically ill child have illustrated that over-protectiveness has detrimental effects on growing child such as symptoms of depression and oppositional behavior. Over-protective parents are also less expected to allow independence to their child in the future. Parents may find it difficult to choose between allowing self-sufficiency to their child and the need to protect the child from injuries and further medical harm. A review done by Giordano et al. [20] showed that children with hemophilia should be allowed self-sufficiency and be encouraged to participate in physical activities such as swimming, walking, and running to strengthen the muscles and joints. Hemophiliac patients should also be informed of their illness so

Table 4 Comparison between the parent Haemo-QoL score dimensions among the different age groups

Dimensions	Parent			Test of sig	*P*
	Group I (4–7 years)	Group II (8–12 years)	Group III (13–16 years)		
Physical health					
Min-max	31.2–81.2	46.4–96.4	53.5–96.4	$^{KW}\chi^2$=11.286	0.004*
Mean ±SD	60.23±15.61	73.9±11.36	78.23±11.85		
Feeling					
Min-max	16.6–83.3	14.2–89.2	43.7–87.5	$^{KW}\chi^2$=3.008	0.222
Mean ±SD	55.90±13.32	63.78±15.97	67.93±12.59		
View					
Min-max	25–62.5	5.5–88.8	45–87.5	$^{KW}\chi^2$=15.271	<0.001*
Mean ±SD	42.85±14.47	63.5±18.95	69.16±16.28		
Treatment					
Min-max	37.5–100	32.1–92.8	18.7–96.8	$^{KW}\chi^2$=0.909	0.635
Mean ±SD	72.32±18.46	65.87±15.76	62.96±24.18		
Sports and school					
Min-max	33.3–91.6	43.7–93.7	39.1–88.8	$^{KW}\chi^2$=5.868	0.053
Mean ±SD	60.08±18.53	74.31±10.90	73.55±17.33		
Other persons					
Min-max	25.0–75.0	12.5–70.8	25.0–87.5	$^{KW}\chi^2$=3.578	0.167
Mean ±SD	51.78±18.25	50.65±15.02	62.12±17.44		
Friends					
Min-max	25.0–75.0	18.7–87.5	25.0–81.2	$^{KW}\chi^2$=4.672	0.097
Mean ±SD	55.35±14.47	45.29±15.67	62.99±19.48		
Family					
Min-max	43.7–100	8.0–90.0	62.5–90.6	$^{KW}\chi^2$=0.277	0.871
Mean ±SD	74.52±15.02	72.41±17.38	76±8.55		
Dealing					
Min-max		21.4–85.7	25.0–71.4	*Z*=0.254	0.800
Mean ±SD		62.60±13.52	61.86±13.72		
Perceived support					
Min-max		6.2–75.0	43.7–87.5	*Z*=0.615	0.538
Mean ±SD		54.67±18.36	61.44±13.55		
Future					
Min-max			37.5–100		
Mean ±SD			65.6±18.74		
Relationships					
Min-max			25–100		
Mean ±SD			68.75±25.28		

Haemo-QoL Haemo quality of life

$^{KW}\chi^2$ chi-square for Kruskal-Wallis test, *Z* for Mann-Whitney test

*Statistically significant at $P \leq 0.05$

that they can manage their future and be able to adapt to their environment accordingly.

Parent responses to Haemo-QoL revealed significantly difference in group three children in the dimension of physical health this may explained as with advancing age recurrent joint bleeding led to worsening of joint health; consequently, their children found it difficult to lead to a normal life with their sick body.

On the other hand, group two children showed least impairment in the dimension of friends; we can conclude that the disease had no negative effect on their friend relationships. Least impairment in the dimension of dealing was present in group three children as they became

Table 5 Relation of Haemo-QoL and HJHS with patients' data

	Child Haemo-QoL (*n*=50)	Parent Haemo-QoL (*n*=50)	HJHS (*n*=50)
Factor activity level			
Moderate	53.45±10.56	57.96±10.96	8.19±3.02
Severe	71.45±7.54	71.83±7.80	12.43±3.51
***T* test (*P* value)**	−5.070 (<0.001)*	−6.778 (<0.001)*	−4.596 (<0.001)*
Duration of hemophilia Correlation coefficient (*P* value)	0.39 (0.006)*	0.41 (0.003)*	0.73 (<0.001)*
Number of bleeding attacks last year Correlation coefficient (*P* value)	0.75 (0.006) *	0.69 (<0.001)*	0.73 (<0.001)*
Duration of joint disease Correlation coefficient (*P* value)	0.427 (0.002)*	0.417 (0.003)*	0.733 (<0.001)*
Number of joints affected Correlation coefficient (*P* value)	0.502 (<0.001)*	0.488 (<0.001)*	0.722 (<0.001)*

Haemo-QoL Haemo quality of life, *HJHS* hemophilia joint health score

* Statistically significant at $P \leq 0.05$

Table 6 Comparison between age groups with Haemo-QoL score of child and parent and HJHS

	Group one (*n*= 14)	Group two (*n*=24)	Group three (*n*=12)	Total (*n*= 50)	Test of significance
Child Haemo-QoL score					
Min-max	28.5–83.3	29.6–80.8	37.9–82.7	28.5–83.3	*F*=1.497
Mean± SD	57.94±15.78	61.49±10.14	66.64±13.90	61.73±12.96	*P*=0.234
Parent Haemo-QoL score					
Min-max	33.3–80.9	30.0–82.0	43.8–83.7	30–83.70	*F*=1.334
Mean± SD	60.75±13.75	64.46±10.29	68.29±12.01	64.34±11.83	*P*=0.273
HJHS					
Min-max	4–10	3–17	4–18	3–18	*F*=9.843
Mean± SD	7.14±2.03	10.54±3.46	12.93±4.13	10.14±3.87	*P* <0.001*

Haemo-QoL Haemo quality of life, *HJHS* Hemophilia Joint Health Score

*Statistically significant at $P \leq 0.05$

responsible for their illness and had better dealing and better understanding of their illness as well as the necessity for factor infusions and supportive measures when bleeding occurs.

In the present study, there was a negative significant relation between child and parent Haemo-QoL and HJHS with severity of hemophilia (*P* value<0.001). Moreover, there was a positive significant correlation between child and parent Haemo-QoL and HJHS with duration of the disease, number of bleeding attacks last year, duration of joint disease, and number of joints affected.

These may be interpreted by the fact that severity of the disease lead to repeated attacks of bleeding and as the children in the present study receive only on-demand therapy in the form of plasma transfusion with infrequent factor transfusion due to financial factors, more damage to joints occur. Also, as the disease progress over years, the joints are subjected to more injury leading to higher scores in the HJHS and more impairment in function that negatively affect their quality of life. This was supported by the study of Espaldon et al. [21].

Poon et al. [22] demonstrated that individuals with more severe hemophilia and higher self-reported joint pain and motion limitation had poorer HRQoL scores, particularly in the physical aspects of HRQoL. The severity of the disease may influence joint movement, physical activity, treatment, and relationships with others, and these factors had a negative impact on the QoL. The presence of chronic synovitis has a significant negative impact on HRQoL in patients with severe hemophilia [23, 24]. Furthermore, patients with a highly impaired orthopedic status had significantly worse HRQoL, as measured by Haem-A-QoL compared to those with a less impaired orthopedic status, indicating the important role of the level of arthropathy to the perceived quality of life [25]. Consistent with the aforementioned reports is the presence of positive significant correlations between child and parent Haemo-QoL with HJHS scores in our studied

patients. So prevention, early diagnosis, and treatment of hemophilic joint should be an important consideration for clinicians and patients when managing hemophilia to improve patient's quality of life.

From all sociodemographic data of the studied patients only mother education had a significant relation with Haemo-QoL of child and parent. Mothers were the main care giver of their hemophilic child. Espaldon et al. [21] found that there was no relation between Haemo-QoL as a score of quality of life and socio-economic status of the families of 51 Filipino children studied.

Knobe et al. [2] showed that recurrent joint bleeding causes synovial proliferation and inflammation (hemophilic synovitis) that contribute to end-stage degeneration (hemophilic arthropathy), with pain and limitation of motion.

Patients with hemophilic arthropathy, especially in severe cases, also suffer from frequent internal blood loss within the joints, which lead to deposition of iron in the synovium. The vulnerability of hemophiliac joints to recurrent bleeding is related to the role of synovial cells and chondrocytes as producers of the tissue factor pathway inhibitor, which aggravates the bleeding tendency within the joints. However, synovial iron deposits are not physiologically functional as they are not readily available for hemoglobin synthesis, but rather they are pathological mediators of inflammatory changes leading to crippling synovitis and arthropathy [26]. Therefore, increased synovial iron stores in hemophiliac patients cannot possibly compensate for the iron deficiency resulting from external blood loss and the depletion of normal storage compartments such as the liver and the bone marrow. It can thus be reasonably predicted that hemophilic arthropathy would be causally related to iron deficiency, a condition that could potentially have an adverse impact on the clinical status of the hemophilic patient [27]. Iron deficiency anemia has not been studied adequately in hemophilia.

A special concern with regard to iron deficient hemophiliac children is the fact that iron deficiency is associated with adverse cognitive and psychological effects, which can lead to attention deficit, social withdrawal, and poor intellectual attainment in school. The intelligence quotients (IQs) of school children deficient in iron are reported to be significantly lower than those of non-anemic peers [28]. This may explain the effect of anemia on school and view dimensions of Haemo-QoL questionnaire found in our study. It is therefore imperative that patients with HA should be screened regularly for iron deficiency so that affected patients can be identified promptly and treated.

Hepatitis C virus (HCV) infection affects HRQoL through fatigue, psychological effects (i.e., depression and cognitive impairment), and stigma [29]. In a cross-sectional study on HRQoL among persons with hemophilia, it was found that hemophilia patients infected with HCV scored lower on the HRQoL domains of general health and vitality than hemophilia patients who had never been infected with HCV [30].

In reviewing literatures, no previous studies were found on quality of life in children infected with HCV; all studies found were conducted on adult population.

Improvement in specific dimensions of quality of life in patients that underwent synovectomy may be explained by the effect of synovectomy on halting the bleeding cycle and improving the range of motion later on thus improving the physical health, treatment, and sports and school dimensions of quality of life. Also reduction of the synovial tissue through synovectomy results in improving pain control that is expressed in feeling, and viewing and dealing dimension improvement.

Conclusion

The quality of life in patients with hemophilic arthropathy was influenced by the joint health, factor activity level, disease duration, number of bleeding attacks, number of joints affected (during life), duration of joint disease, and presence of hepatitis C virus.

Abbreviations

HJHS: Hemophilia Joint Health Score; Haemo-Qol: Haemo quality of life; IPSG: International Prophylaxis Study Group; HRQoL: Health-related quality of life; IQs: Intelligence quotients; HCV: Hepatitis C virus.

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Authors' contributions

Study concept and design: HH and HM. Collection of the patients: HR. Examination of the patients and Hemophilia Joint Health Score Assessment by HM. Assessment of function by Haemo quality of life: HR. Analysis and interpretation of data: HH, HR and HM. Drafting of the manuscript: HR and HM. Critical revision of the manuscript for important intellectual content: HH and HM. The authors have read and approved the manuscript.

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Availability of data and materials

Patients were selected from those attending the outpatient clinics of the Hematology and Physical Medicine, Rheumatology and Rehabilitation (Alexandria University Children's Hospital) at El Shatby.

Declarations

Ethics approval and consent to participate

The study was approved by the local ethics committee of the Faculty of Medicine, Alexandria University. The study was explained to the participants and their parents and a written consent was taken from parents of all children included in the study.

Consent for publication
Not applicable.

Competing interests
The authors declare that they have no competing interests.

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