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Health-related Quality of Life in Children and Adolescents With Hemophilia in Basra, Southern Iraq

Murtadha Y. Taha, CABP and Meàad K. Hassan, CABP

Objectives: The aim of this study was to assess health-related quality of life in hemophilic children and adolescents, and describe the impact of health status on quality of life.

Methods: The study included 45 patients with hemophilia A and B, their ages ranged from 4 to 16 years. Health-related quality of life was assessed by Hemophilia Quality of Life Questionnaire (Haemo-QOL) US-English long version for 3 age groups (I: 4 to 7; II: 8 to 12; and III: 13 to 16 y).

Results: The study did not reveal a significant difference in the Hemophilia Quality of Life total score in relation to age of patients. However, young children are mainly impaired in the dimension family; children aged 8 to 12 years are mainly impaired in the dimension sport and adolescents in perceived support. Severity of hemophilia adversely affects the quality of life; patients with severe hemophilia have the highest total score of 58.51 ± 3.62, followed by moderate type 37.55 ± 5.37, and then mild hemophilia 35.47 ± 4.19, $P < 0.05$. Among children with severe hemophilia, young children who had ≥ 5 joint bleeds during the last year have significant impairment in the total score and in several dimensions including physical health, feeling, and treatment compared with children who had < 5 joint bleeds, $P < 0.05$.

Conclusions: Severity of hemophilia adversely affects the quality of life, and clinical severity significantly affects quality of life among patients with severe hemophilia. Thus, the importance of prophylaxis is emphasized in improving the quality of life of our children with hemophilia.

Key Words: hemophilia, quality of life, children and adolescents

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Health-related quality of life (HRQoL), is a multidimensional construct concerned with the physical, emotional, mental, social, and behavioral components of well-being and function as perceived by the patients and/or observers. HRQoL is not only influenced by disease and its treatment but also by personal characteristics such as coping, individuals perception about the underlying main causes of events in his or her life, living conditions, and socioeconomic status.[1]

The quality of life (QoL) of children with chronic conditions has received increasing attention in recent years especially for frequent pediatric health conditions such as asthma or life-threatening conditions such as leukemia. However, the QoL of young people with rare diseases like hemophilia has been largely neglected.[2] It is important to understand more about QoL in this patient population to evaluate and if necessary to improve the care these patients receive.[3]

Application of the different levels of this context to hemophilia include: health condition; the clotting defect, body structures; hemarthrosis and arthropathy, body functions; active range of motion, muscle strength, coordination, activities; personal hygienic care (home treatment with clotting factor),walking riding bicycle, participation; and fulfilling ones social role like taking part in family life, attending school, and employment.[4]

Hemophilic children do not seem to be more at risk of behavioral or socialization problems compared with male age-matched peers. However, some difficulties with emotional well-being have been reported, including depressive symptoms and lower self-perception, although mean scores are generally within normal range.[5]

Frequent absences from school, such as those experienced by children with chronic diseases can interfere with the academic and social development of children. Hemophilia Growth and Development Study (HGDS) report showed associations between prolonged hospitalization and lower achievement test scores in reading and spelling.[6] Integration of boys with hemophilia into normal schools is no longer a problem after the introduction of prophylaxis and home treatment, as confirmed in the Dutch hemophilic population.[7]

In Basra, there is lack of interest and information concerning the QoL of patients with chronic diseases, one of these diseases is hemophilia. Therefore, this study was carried out to assess HRQoL in hemophilic children and adolescents registered at Center for Hereditary Blood Diseases (CHBD) and the impact of their health status on QoL.

PATIENTS AND METHODS

A cross-sectional study has been carried out on patients with hemophilia A and B who have been registered at CHBD in Basra from the first of February to the end of October 2011.

Of the 98 patients, 49 were 4 to 16 years old. A total of 45 patients were included in the study, the other 4 patients were not enrolled in the study because it was not possible to contact them and they did not consult the CHBD during the study period.

The following information were obtained: age, residence, age at first bleeding episode, age at diagnosis, type of hemophilia, severity of disease, previous history of inhibitors development, hepatitis markers, HIV, number of joint bleeding events that required treatment in previous year (less than 5 or more than or equal to 5),[8] presence of

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life-threatening bleeding events throughout the patients' life, and sites (intracranial hemorrhage, neck, iliopsoas).[9]

Patients were also interviewed about the presence of chronic pain (pain of >3 mo duration).[10]

Examination of the joints looking for swelling, muscle atrophy, deformity, and limitation of movement was carried out for all patients.

Information concerning treatment included the place of treatment administration, treatment administrator, and type of product used for treatment, plasma-derived or recombinant.

HRQoL was assessed by newly developed disease-specific HRQoL questionnaires for children with hemophilia, which is Hemophilia Quality of Life Questionnaire (Haemo-QOL), US-English long version for 3 age groups (I :4 to 7; II: 8 to 12; and III: 13 to 16 y).[11] The questionnaire was used as it was in English language. However, the investigators were very well mastered in English language and translated the questions into Arabic while interviewing patients. It has also been shown to local colleagues for consistency.

Parents' long version for smaller children (age group I: 4 to 7 y) was available with 21 items pertaining to 8 dimensions (physical health, feelings, view, family, friends, others, sport and school/kindergarten, treatment). For the school children aged 8 to 12 years (age group II), the self-administered questionnaire consisted of 2 additional domains (perceived support, dealing) with overall 64 items. For adolescents (age group III: 13 to 16 y) it was expanded with 2 further additional domains (relationships, future) and consisted of 77 items.

According to preliminary analyses, the index's psychometric performance concerning reliability and convergent validity of Haemo-Qol for children aged 4 to 16 years old was good.[12]

The Scoring system includes assigning numeric values to the response scale for the age group and recoding positively worded items. Using the Scoring List, it is necessary to identify which items belong to a subscale. Items to be recoded are marked with an "R," summing up the items belonging to a subscale yields the raw score per subscale, comparing scores across subscales (standardized scale score), transferring a raw score to a transformed scale score between 0 and 100, producing the total score of the specific Haemo-QoL age group version.[11] High values indicate high impairments in HRQoL.[9]

Statistical analysis was carried out using SPSS program, version 17. Comparisons of proportions were performed by crosstab using χ^2 test. Analysis was also carried out among multiple groups by using analysis of variance. For all tests, P-value of <0.05 was considered as statistically significant.

RESULTS

Of the 49 patients with hemophilia in the age group of 4 to 16 years, 4 patients were not included in the study. All of them were from peripheries of Basra and belong to families of low socioeconomic level, 2 of them with severe hemophilia, 1 with moderate, and the last patient with mild type. It is most likely that they consult the local hospital in their district during bleeding episode.

Most cases in all age groups were hemophilia A, 14 (93.3 %) for both 4 to 7 years and 8 to 12 years age group and 12 (80%) for age group 13 to 16 years. For hemophilia B, 1 (6.7%) for both 4 to 7 years and 8 to 12 years age group and 3 (20%) for the age group of 13 to 16 years old. Nearly half (21 [46.6%]) of all hemophilic patients had severe hemophilia, followed by mild and moderate (12 [26.7%]) for each type.

The mean age at first bleeding episodes was 8.72 ± 1.76 months with statistically significant difference between mild (14.58 ± 5.61) and severe hemophilia (8.72 ± 1.76), P-value <0.05 (Table 1).

The mean age at diagnosis was 24.36 ± 4.22 months. Patients with severe hemophilia were diagnosed at a significantly younger age (14.92 ± 3.36 mo) compared with those with mild hemophilia (36.91 ± 12.08 mo), P-value <0.05.

Most children included in the study had no life-threatening bleeding episodes (91.1%), although chronic pain was reported in 35.6% and joint impairment in 31.1%.

All children enrolled in the study received on-demand factor replacement therapy.

The mean values (transformed score) of the Haemo-QoL dimensions in the 3 age groups are presented in Figure 1. It demonstrates that youngest children are

TABLE 1. Selected Clinical Variables

Total number	45
Hemophilia A (n [%])	40 (88.9)
Hemophilia B (n [%])	5 (11.1)
Age (y)	
4-7	15
8-12	15
13-16	15
Severity (factor level)	
Mild (5%-20%)	12 (26.7)
Moderate (1%-5%)	12 (26.7)
Severe (0%-1%)	21 (46.6)
Age at first bleeding episodes*	8.72 ± 1.76
Age at diagnosis*	24.36 ± 4.22
Age at first joint bleeding*	26.02 ± 3.58
Joint bleeds (n [%])	
0	8 (17.8)
< 5	19 (42.2)
≥ 5	18 (40)
Life-threatening bleeds (n [%])	
Yes	4 (8.9)
No	41 (91.1)
Chronic pain (n [%])	
Yes	16 (35.6)
No	29 (64.4)
Joint impairment (n [%])	
Yes	14 (31.1)
No	31 (68.9)
Place of therapy administration (n [%])	
Home	3 (6.7)
Hospital	23 (51.1)
Both	19 (42.2)
Type of replacement therapy (n [%])	
Plasma derived	4 (8.9)
Recombinant factor	13 (28.9)
Both	28 (62.2)
Inhibitors (n [%])	
Positive	10 (22.2)
Negative	35 (77.8)
Hepatitis C antibody positivity (n [%])	
Positive	1 (2.2)
Negative	44 (97.8)

*Mean age (mo) ± SD.

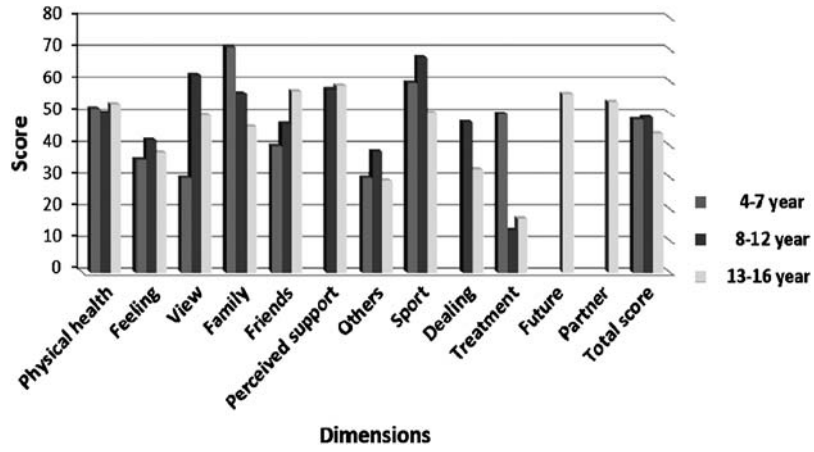

FIGURE 1. Haemo-QoL scores (transformed data) among hemophilic patients in relation to age. Haemo-QoL indicates Hemophilia Quality of Life Questionnaire.

mainly impaired in the dimension family (70.833 ± 8.768), followed by sport dimension (59.960 ± 7.240).

Children in the age group of 8 to 12 years were mainly impaired in the dimension sport (67.673 ± 4.625) followed by view dimension (62.206 ± 4.992). However, children in the age group of 13 to 16 years are mainly impaired in the dimension perceived support (58.750 ± 3.439) followed by friends dimension (57.066 ± 7.562).

The study revealed that children with mild hemophilia are mainly impaired in the dimension sport (61.058 ± 7.432), followed by perceived support dimension (59.722 ± 4.181) (Fig. 2).

Children with moderate hemophilia were mainly impaired in the dimension partner (57.000 ± 14.543) followed by perceived support dimension (53.125 ± 2.891), whereas children with severe hemophilia were mainly impaired in the dimension future (76.041 ± 7.809) followed by partner dimension (72.500 ± 11.456).

Among children with severe and mild hemophilia, it was found that there was a significant impairment in the total score (58.51 ± 3.62 vs. 35.47 ± 4.196), and in the dimensions physical health, feeling, view, family, others, treatment, future, and partner among children severe hemophilia compared with those with mild hemophilia, $P < 0.05$, whereas for children with severe and moderate hemophilia, there was a significant impairment in the total score (58.51 ± 3.62 vs. 37.550 ± 5.371), and in the dimensions physical health, feeling, view, family, and sport among children with severe hemophilia compared with those with moderate hemophilia, $P < 0.05$.

Children with severe hemophilia aged 4 to 7 years who had ≥ 5 joint bleeds during the last year had a significant impairment in the total score, and in the dimensions physical health, feeling, and treatment compared with 3 children who had < 5 joint bleeds, $P < 0.05$ (Table 2).

Among children aged 13 to 16 years, 4 children had ≥ 5 joint bleeds in the last 12 months. These patients had more impairment in QoL in comparison with 2 children with < 5 joint bleeds in the dimension treatment, *P*-value < 0.05.

Among patients with severe hemophilia, life-threatening bleeds throughout patients life are associated with differences in Haemo-QoL scores in comparison with those with no life-threatening bleeds (Table 3). It reveals that children with severe hemophilia and life-threatening bleeds are more impaired in their HRQoL in the dimension view in comparison children who have no life-threatening bleeds, *P*-value < 0.05, whereas those who had no life-threatening bleeds were more impaired in the dimension dealing, *P*-value < 0.05.

All patients were screened for inhibitors. The study revealed that 35 (77.8%) patients were negative for

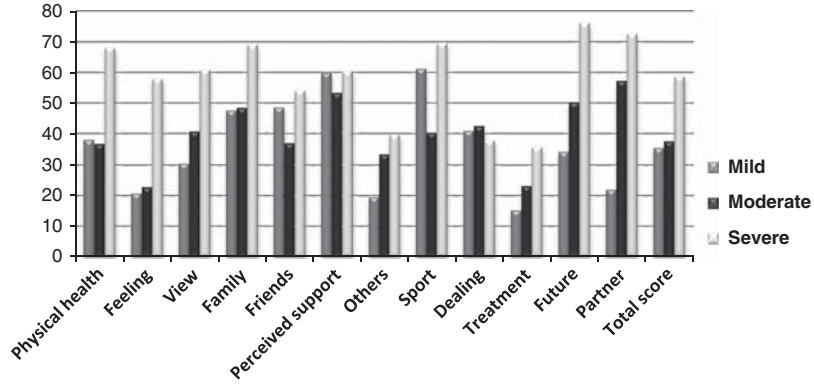

FIGURE 2. Haemo-QoL scores (transformed data) according to severity of hemophilia. Haemo-QoL indicates Hemophilia Quality of Life Questionnaire.

TABLE 2. Haemo-QoL Scores Among Patients With Severe Hemophilia of Different Age Groups in Relation to Number of Joint Bleeds

	Age (y)								
	4-7 (N = 8)			8-12 (N = 7)			13-16 (N = 6)		
	No. of Joint Bleeding								
Haemo-QoL Dimension*	5 < (N = 3)	≥5 (N = 5)	*P*	< 5 (N = 3)	≥5 (N = 4)	*P*	5 < (N = 2)	≥5 (N = 4)	*P*
Physical health	45.83 ± 8.333	80.00 ± 10.15	< 0.05	45.20 ± 22.69	71.40 ± 18.96	> 0.05	75.00 ± 0	79.45 ± 7.05	> 0.05
Feeling	16.60 ± 0.53	79.98 ± 16.171	< 0.05	55.93 ± 28.43	73.15 ± 7.39	> 0.05	62.50 ± 12.50	42.95 ± 3.46	> 0.05
View	25.00 ± 0.54	55.00 ± 12.24	> 0.05	65.66 ± 17.65	73.92 ± 7.26	> 0.05	73.75 ± 3.75	71.25 ± 4.14	> 0.05
Family	62.33 ± 19.09	90.00 ± 6.12	> 0.05	63.33 ± 11.66	70.00 ± 7.35	> 0.05	68.70 ± 9.40	50.76 ± 6.54	> 0.05
Friends	50.00 ± 0.56	60.00 ± 10.00	> 0.05	23.50 ± 13.31	64.06 ± 11.97	> 0.05	43.75 ± 0	67.18 ± 19.32	> 0.05
Perceived support	—	—	—	50.68 ± 8.87	60.93 ± 5.91	> 0.05	65.62 ± 9.37	64.06 ± 8.97	> 0.05
Others	25.00 ± 0.55	45.00 ± 14.75	> 0.05	44.43 ± 18.6	46.85 ± 4.92	> 0.05	41.65 ± 8.35	30.15 ± 3.93	> 0.05
Sport	55.53 ± 14.69	73.28 ± 6.68	> 0.05	63.53 ± 7.29	80.37 ± 11.35	> 0.05	62.45 ± 6.95	71.27 ± 21.22	> 0.05
Dealing	—	—	—	33.26 ± 9.75	58.00 ± 8.54	> 0.05	32.10 ± 3.60	24.08 ± 6.56	> 0.05
Treatment	41.66 ± 8.33	75.00 ± 7.90	< 0.05	10.66 ± 10.66	24.05 ± 9.47	> 0.05	9.33 ± 0.03	25.70 ± 1.47	< 0.05
Future	—	—	—	—	—	—	65.62 ± 9.37	81.25 ± 10.52	> 0.05
Partner	—	—	—	—	—	—	50.00 ± 25.00	83.75 ± 9.86	> 0.05
Total score	41.25 ± 5.55	73.76 ± 7.48	< 0.05	49.56 ± 11.07	62.30 ± 8.90	> 0.05	55.10 ± 0.90	57.02 ± 3.24	> 0.05

*Values are expressed as mean ± SD.
Haemo-QoL indicates Hemophilia Quality of Life Questionnaire.

inhibitors and 10 (22.2%) were positive for inhibitors, 5 (50%) of them in the age group of 8 to 12 years. There was no significant difference in the HRQoL dimensions and total score in relation to the presence or absence of inhibitors (*P*-value > 0.05, Fig. 3).

DISCUSSION

HRQoL has been regarded as an important outcome factor in hemophilia. However, only few papers have discussed the question, which factors might positively or negatively affect the QoL of children with hemophilia and how might these differ between different countries.[2]

Many instruments to measure QoL in hemophilia have been constructed over the last few years. In the current study the HRQoL was assessed by newly developed disease-specific long version Haemo-QoL questionnaires for 3 age groups. The questionnaire includes many dimensions that involve almost all the aspects of the well-being of children with hemophilia of different age groups[13]; these dimensions are presented in Table 4.

TABLE 3. Life-threatening Bleeds and HRQoL

	Life-threatening Bleeds		
Haemo-QoL Dimensions*	Yes (N = 4)	No (N = 17)	*P*
Physical health	78.55 ± 7.58	65.42 ± 7.08	> 0.05
Feeling	65.37 ± 11.58	55.61 ± 8.29	> 0.05
View	77.75 ± 3.26	56.71 ± 5.79	< 0.05
Family	55.45 ± 9.05	72.12 ± 5.06	> 0.05
Friends	45.31 ± 19.32	55.98 ± 5.65	> 0.05
Perceived support	56.25 ± 7.65	62.03 ± 5.20	> 0.05
Others	37.45 ± 8.52	39.96 ± 6.90	> 0.05
Sport	76.37 ± 9.11	67.62 ± 5.95	> 0.05
Dealing	20.51 ± 6.2	45.58 ± 5.64	< 0.05
Treatment	15.57 ± 6.61	40.43 ± 6.90	> 0.05
Future	66.66 ± 13.66	85.41 ± 5.51	> 0.05
Partner	83.33 ± 8.33	61.66 ± 21.66	> 0.05
Total score	57.87 ± 3.84	58.66 ± 4.42	> 0.05

*Values are expressed as mean ± SD.
Haemo-QoL indicates Hemophilia Quality of Life Questionnaire; HRQoL, health-related quality of life.

Age of the patient was not found as a strong factor affecting the HRQoL of hemophilic patients in this study, in the total score in addition to both physical dimensions and social dimensions. This is in contrast to the study in Italy by Scalone et al,[14] in which HRQoL was assessed by 2 generic and self-administered questionnaires: the EuroQol instrument (EQ-5D) and the Short Form-36 (SF-36), wherein the overall quality of life was negatively associated with age in both questionnaires. However, young children are mainly impaired in family dimension and older children in sport and perceived support. This is in agreement to that reported in other studies.[1,9] This can be explained by the overprotection of parents, for young children, assessed in the dimension family, whereas older children had higher impairments in the social dimensions, such as perceived support.

The present study confirmed that the severity of hemophilia adversely affects HRQoL in the majority of the dimensions; this is similar to the study in the United Kingdom by Miners et al,[15] who reported that compared with individuals with moderate/mild hemophilia and the UK male normative population, individuals with severe hemophilia generally recorded poorer levels of HRQoL. This may be related to high morbidity associated with severe hemophilia, especially in the absence of prophylactic therapy.

Among patients with severe hemophilia, HRQoL mean scores exceeded 50 for all age groups. This is in agreement with the results of Tantawy et al[16] in Egypt, which reported a mean score above 50. However, other studies in Turkey by Mercan et al[17] reported a better score (39.6 ± 15), and in Europe by Gringeri et al,[9] in which the mean scores were widely below 30. In addition, Bullinger and colleagues in a multicenter study found that mean total score in France was 25.93 ± 7.6, followed by Spain 22.49 ± 11.17; less impairments were reported by children in Germany (19.26 ± 8.2) and Italy (21.95 ± 10.2). Significant differences were shown between the countries in

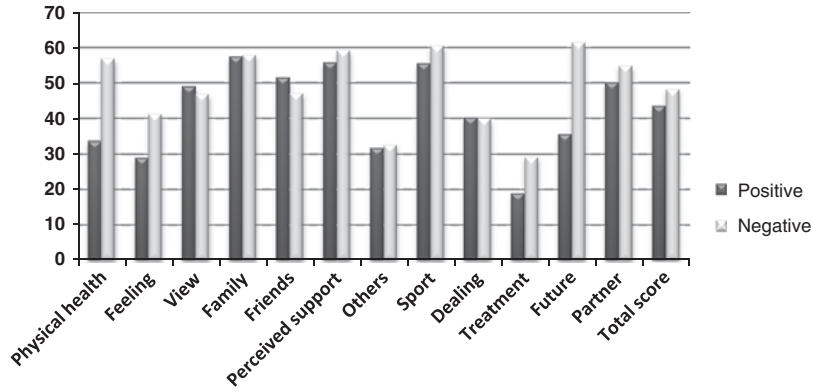

FIGURE 3. Inhibitors and HRQoL. HRQoL indicates health-related quality of life.

almost all subscales as well as for the total Haemo-QoL score; these results showed that psychosocial factors affecting QoL include coping, social support, and locus of control in contrast to clinical variables, which contribute highly to the explained variance, differing across countries.[2] The variation in QoL impairments could be related to reduced life satisfaction and a high number of major bleedings. Many factors like severity of disease, number of bleeding episodes, and type of treatment (prophylactic versus on-demand), which are important predictors, depend on the health care system and specific characteristics of a given country.[2]

The view dimension assesses how children perceive themselves (perceived competence); this means that children and adolescents with severe hemophilia have negatively perceived themselves. This is in contrast to study in Netherland by Hegemen et al,[18] in which children and adolescents with hemophilia in general have a perceived competence that is comparable to that of healthy peers. This may be explained by lack of prophylaxis, leading to restriction of children with hemophilia to participate in physical activities.

Higher impairment for children with >5 joint bleeds in the previous 12 months in the dimensions physical health, feeling, and treatment, yielding a significant difference in the total score was reported in this study, especially among young children. This is in contrast to study in Europe by Von Mackensen et al,[8] in which differences appeared, especially in the older age groups, in the dimensions physical health, view, perceived support, and, especially, sports activity, and in the total score, whereas Scalone et al[14] in Italy did not report a significant association between the patients' HRQoL and the bleeding frequency. This clearly indicates that in addition to clinical characteristics, indicated by poor physical health perception, psychosocial predictors and social support are also important and could explain the variance among different countries.

The presence or absence of life-threatening bleeding among patients with severe hemophilia is not associated with significant difference in HRQoL in the total score; this in contrast to study in Europe by Gringeri et al,[9] in which a slightly lower HRQoL score was observed in smaller children with less major bleeding events, which were clearly associated with prophylactic treatment, whereas HRQoL tested better in adolescents with less bleeding events. These findings indicate strongly that the initial burden induced by prophylaxis in younger children is highly compensated by improvements in HRQoL in older children.

In this study, HRQoL was not affected by the presence of inhibitors; this was similar to findings of Scalone et al[14] in Italy and Tantawy et al[16] in Egypt. This could be attributed to be effective strategies used for the management of this complication, which is perceived as satisfactory by patients, who seem to cope well with their experience of inhibitor development.[2]

From this study it can be concluded that the use of home therapy and prophylaxis are important to improve HRQol among our children with hemophilia as the severity of hemophilia, and major bleeding episodes, adversely affect Haemo-QoL scores among patients with severe hemophilia. This could explain the lower HRQol scores compared with countries who adopted prophylactic therapy for these patients.

TABLE 4. Haemo-QoL Questionnaire Dimensions[9,11]

Dimension	Concept
Physical	Questions are related to pain and bleeding, walking and joints stiffness
Feeling	Concerns how children feel related to their hemophilia
View	This dimension is about how children perceive themselves
Family	It includes questions about the interaction in the family
Friends	Contains questions about the interaction with friends
Perceived support	Questions are about how children perceive the support they receive from others
Sport and school	Children are asked about their school life
Dealing	Contains questions about how children deal with their hemophilia
Treatment	Is concerned with treatment issues like injections and visiting hemophilia center
Others	The interaction with others is investigated in this dimension
Future and partnership	Ask about specific issues, such as leading normal life in the future

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