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Health-Related Quality of Life in Children with Hemophilia A: A Single Center Study from Vietnam

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ABSTRACT: Hemophilia A (HA) is a disease of inheritance, stated as a factor VIII deficiency. Despite low incidence, HA usually involves repeated bleeding episodes leading to joint damage and negative impact on patients' HR-QoL. This analysis aimed to assess the HR-QoL in children with HA and influential factors on their HR-QoL. A study of cross-section was done to examine HR-QoL in all children of HA, hospitalized at Children's Hospital. Face-to-face interview with patients and their parents has been conducted using Peds-QL 4.0 SF-15 questionnaire from January to June, 2018. Data were analyzed in SPSS using relevant statistical test with 95% confidence level. 126 patients with the mean age of 10.8 ± 4.0 years have been chosen for the study and classified into 3 groups: 5-7 years (27.8%), 8-12 years (32.5%) and 13-18 years (39.7%). 50.8% of patients had severe disease status, 65.9% had bleeds in the joints with average disease duration of 9.67 ± 4.33 years and average treatment period of 4.6 ± 4.3 days. The mean Peds-QL scores were assessed from both patients and parents with 64.9 ± 15.7 and 64.0 ± 16.5, respectively in group I, 58.6 ± 17.1 and 56.1 ± 17.0 in group II; and 53.7 ± 15.5 and 51.2 ± 14.7 in group III. Age, disease, duration, education level, and site of bleeding were influential factors on HR-QoL. HA has moderate impact on HR-QoL of children with more impact on the physical health than psychosocial health.

Keywords: Hemophilia A, life quality, children, adolescents, Peds-QL, Vietnam.

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INTRODUCTION

Hemophilia A (HA) is a disease of inheritance that results in factor VIII (FVIII) levels and manifestation of bleeding throughout life that especially causes permanent damage of the bone joints. Normal ranges for factor VIII levels are from 50% to 150%. If your factor VIII activity level is less than 50%, you may have hemophilia A, but how severity of risk of bleeding depends on what is the percentage of factor VIII levels (St-Louis *et al.*, 2016).

Globally, HA is spread approximately 1/5,000 male individuals, with approximately 1/3 of having effects on people not inheriting it from family (World Federation of Haemophilia, 2016; Tantawy *et al.*, 2011). The estimated number of people having HA is 151,159, which was on the basis of the World Federation of Hemophilia (WFH) survey in the year 2015 (Konkle *et al.*, 2004). The prevalence of HA various according to the reporting country with 6,000 hemophilic patients and 30,000 carriers estimated in Vietnam in 2016 (Bộ Y tế, 2016). Because of the deficiency of FVIII activity, they may bleed spontaneously, often in the joints, muscles, mucous membranes in mouth, gums, nose even central nervous system or gastrointestinal, resulting in life-threatening complications, especially in patients with severe/moderate HA.

Moreover, hemarthrosis can cause the progressive destruction of hinge joints, bone and affecting the joint function (Srivastava *et al.*, 2013). This is a major reason of the morbidity contributing to disability of HA patients. These manifestations negatively impact not only the physical health of patients with HA but also their psychosocial well-being, leading to the significant decrease of their HR-QoL.

Currently, all over the world, many studies assessing the HR-QoL in HA patient have been conducted in many countries such as Egypt, USA, China, Canada, Netherlands, Australia, and Sweden. HR-QoL of children is influenced by severity of hemophilia, bleeding rates, physical activity restriction, financial burden and treatment. HR-QoL assessment provides a comprehensive vision of the patient's subjective feelings of function and well-being, and supports evaluation of therapeutic effect (World Federation of Haemophilia 2016; Poon *et al.*, 2012; Wang *et al.*, 2004, Revel-Vilk *et al.*, 2004; Van der Net, *et al.*, 2006; Broderick *et al.*, 2010; Dekoven *et al.*, 2013). This topic on HR-QoL of HA patients are limited in Vietnam. The aim of this research is to assess HR-QoL in children admitted to Children's Hospital in Vietnam with HA and determining the influential factors on their HR-QoL using the hospital's database.

MATERIALS AND METHODS

A. Design of study and collection of data

All children with HA treated at Children's Hospital of Ho Chi Minh City (HCMC), satisfying the inclusive and exclusive data (Table 1) were recruited into this study.

Face-to-face interview with each patients and their parents was conducted using Peds-QL 4.0 SF-15 questionnaire from January to May 2018. Information regarding clinical characteristics such as severity, comorbidities, site of bleeding, disease duration and treatment hospitalization were derived from medical records of the patients.

Table 1: Inclusion and exclusion criteria.

Inclusion criteria	Exclusion criteria
- Patients were diagnosed with HA (D66) - Aged 5-18 years old - Agreed to participate in this study - They were able to answer the questionnaire	- Did not complete the questionnaire - Did not complete their treatment process

B. Peds-QL 4.0 SF-15 questionnaire

The Peds-QL is a generic instrument of HR-QoL, which is not specific on diseases for measuring HR-QoL in children within the age of 2-18 years, consisting of self-reports of child and proxy report of parents. The Peds-QL 4.0 SF-15 includes 15 questions that assess 2 core dimensions with 4 functioning of HR-QoL: physical health) and psychosocial health. Patients and their parents were scored on a 5-point scale based on the frequency of them facing issues in the past four weeks from 0-4 or 3-point scales for the self-report of young. The score was calculated by changing the scores of every dimension and also the score in total, on a range of scale of 1-q 100, 0 to 100 with higher scores, thus indicating better HR-QoL (Varni *et al.,* 2001; Varni *et al.,* 1999).

C. Statistics

SPSS 20.0 was used to derive data. Statistics of description was put to use for characterizing the study population (presented by mean deviation and standard deviation or frequency and percentage). Relevant statistical tests such as T-test, ANOVA, and Pearson correlation were utilized for determining influencing factors on HR-QoL scores. For all tests, P-value of < 0.05 was taken to be statistically significant.

RESULTS

The study sample included 126 HA patients, hospitalized because of disease from January to May 2018 at Children's Hospital of HCMC with the characteristics as shown in Table 2.

Study samples, including 126 male children were classified into 3 groups: 5-7 years (27.8%); 8-12 years (32.5%) and 13-18 years (39.7%) with the mean age of 10.8 ± 4.0 yrs. Educational level was relevant to age group with 23% at lower primary level, 32.5% at primary, 35.7% at secondary and 8.7% at high school level. Among 126 patients, 41.3% patients had family history and 15.1% patients had comorbidities such as bronchitis, asthma, osteoarthritis, heart disease, liver, stomach, kidney disease and other diseases.

Table 2: The demographic and clinical characteristics of patients.

Characteristics	Number (%)/ Mean (SD)
Male	126 (100)
Female	0 (0)
< Primary education level	29 (23.0)
Primary	41 (32.5)
Secondary	45 (35.7)
High school	11 (8.8)
I: Young children (5-7)	35 (27.8)
II: Children (8-12)	41 (32.5)
III: Teens (13-18)	50 (39.7)
Severe Hemophilia A	51 (40.5)
Moderate Hemophilia A	64 (50.8)
Mild Hemophilia A	11 (8.7)
Comorbidities	19 (15.1)
No commorbities	107 (84.9)
Family history	52 (41.3)
Joint bleeds	83 (65.9)
Mucous membranes in the mouth, gums, nose	28 (22.2)
Muscle bleeds	9 (7.1)
Other bleeds	6 (4.8)
Treatment hospitalization period (days)	4.60 (4.25)
Age (years)	10.8 (4.03)
Disease duration (years)	9.67 (4.33)

With mean disease duration of 9.67 ± 4.33 years and hospitalization of 4.60 ± 4.25 days, most of the patients had joint hemorrhages (65.9%); 22.2% suffered from bleeding into mucous membranes such as mouth, gums and nose; 7.1% suffered from muscle bleed and 4.8% from hemorrhage at other sites. When classified by disease severity, mild, moderate and severe patients were 8.7%, 50.8% and 40.5%, respectively.

A. HR-QoL from patients' and parents' report

The HR-QoL of children with HA was assessed with Peds-QL questionnaire survey from both patients and their parents. The mean HR-QoL scores reported by patients and their parents are presented in Table 3.

From patients' report it has been shown that physical health has lower HR-QoL score than psychosocial health in group I (46.4 ± 28.4 vs 74.6 ± 15.3), group II (41.3 ± 9.0 vs 67.6 ± 16.0) and group III (29.1 ± 19.9 vs 66.3 ± 16.6). Psychosocial health in 3 age groups have high HR-QoL score with value range from 66.3 ± 16.6 (group III) to 74.6 ± 15.3 (group I).

In functions of psychosocial health, social functioning has highest HR-QoL score in 3 groups with value of 86.0 ± 16.4 in group I, 83.8 ± 18.4 in group II and 84.7 ± 19.3 in group III. School functioning has HR-QoL score in the second rank in group I (75.5 ± 26.0) and group III (60.9 ± 26.7). Emotional functioning has the lowest HR-QoL score among psychosocial health functions in group I (64.9 ± 22.4) and group III (56.5 ± 21.0) and the same score with school functioning in group II (61.0 ± 24.3 vs 61.0 ± 24.3, respectively).

Table 3: Mean scores for health-related quality of life from patients' report.

	Age group I (5-7 years) N= 35	Age group II (8-12 years) N= 41	Age group III (13-18 years) N= 50	p-value
Mean scores for health-related quality of life from patients' report (Mean (SD))				
Physical health	46.4 (28.4)	41.3 (9.0)	29.1 (19.9)	0.006
Psychosocial health	74.6 (15.3)	67.6 (16.0)	66.3 (16.6)	0.053
Emotional functioning	64.9 (22.4)	61.0 (24.3)	56.5 (21.0)	0.233
Social functioning	86.0 (16.4)	83.8 (18.4)	84.7 (19.3)	0.872
School functioning	75.5 (26.0)	60.1 (26.4)	60.9 (26.7)	0.020
Total HR-QoL score	64.9 (15.7)	58.6 (17.1)	53.7 (15.5)	0.009
Mean scores for health-related quality of life from parents' report (Mean (SD))				
Physical health	44.6 (29.1)	35.6(25.5)	27.6(19.1)	0.008
Psychosocial health	74.1 (14.6)	66.6 (18.2)	63.2 (16.0)	0.012
Emotional functioning	68.2 (19.3)	61.7 (23.9)	56.5 (22.7)	0.060
Social functioning	85.3 (18.1)	78.7 (18.5)	77.9 (14.1)	0.166
School functioning	70.5 (23.4)	61.3 (26.9)	57.5 (24.7)	0.066
Total HR-QoL score	64.0 (16.5)	56.1 (17.0)	51.2 (14.7)	0.002

From patients' report, the total HR-QoL scores has been found to be moderate in 3 groups with decrease from group I to group III with 64.9 ± 15.7, 58.6 ± 17.1 and 53.7 ± 15.5, respectively. The difference in HR-QoL scores has been found to be statistical significant between group I and III from patients' report (64.9 ± 15.7 vs 53.7 ± 15.5, p= 0.006). Furthermore, the study indicated that difference which was statistically significant was seen between HR-QoL score of physical health in group I and III (46.4 ± 28.4 vs 29.1 ± 19.9, p = 0.007). Meanwhile, school functioning shows the significant difference not only between group I and II (75.5 ± 26.0 vs 60.1 ± 26.4, p = 0.033) but also between group I and III (75.5 ± 26.0 vs 60.9 ± 26.7, p = 0,036).

The same picture of HR-QoL value has been found when interviewing the parents. According to the parents' report, patients in three age groups showed lower HR-QoL score on physical health in comparison with psychosocial health: 44.6 ± 29.1 vs 74.1 ± 14.6 in group I, 35.6 ± 25.5 vs 66.6 ± 18.2 in group II, and 27.6 ± 19.1 vs63.2 ± 16.0 in group III. The HR-QoL scores of psychosocial health in three age groups were high; in which, social functioning gets the highest value of 85.3 ± 18.1 in group I, 78.7 ± 18.5 in group II and 77.9 ± 14.1 in group III. In two remaining functions of psychosocial health, school functioning showed the highest HR-QoL scores than emotional functioning in group I (70.5 ± 23.4 vs 68.2 ± 19.3) and group III (57.5 ± 24.7 vs 56.5 ±22.7), whereas in group II the HR-QoL score of these two functions was approximately equal (61.7 ± 23.9 compared to 61.3 ± 26.9). Similar to children's report, it has been found that patients in three age groups had moderate HR-QoL scores with the decreasing values as follows: 64.0 ± 16.5 (group I), 56.1 ± 17.0 (group II) and 51.2 ± 14.7 (group III).

The difference in HR-QoL scores has been found to be statistical significant between group I and III as stated by the parents' report (64.0 ± 16.5 vs. 51.2 ± 14.7, p = 0.001). In addition, HR-QoL score in two dimensions of HR-QoL also showed statistically significant difference between group I and III: physical health (44.6 ± 29.1 vs 27.6 ± 19.1, p = 0.006) and psychosocial health (74.1 ± 14.6 vs 63.2 ± 16.0, p =0.009).

The study found that there was a strongly positive correlation between HR-QoL scores from patients' report and from parents' report with $r > 0$ and $p < 0.05$. More detail about Pearson correlation coefficients and p-value are illustrated in Table 4 and Fig. 1.

Table 4: Correlation coefficients between HR-QoL scores from patient's and parent's report.

	Age group I (5-7 years) N= 35		Age group II (8-12 years) N= 41		Age group III (13-18 years) N= 50	
	r	P-value	R	P-value	r	P-value
Physical health	0.889	0.000	0.927	0.000	0.946	0.000
Psychosocial health	0.483	0.003	0.782	0.000	0.863	0.000
Emotional functioning	0.335	0.049	0.693	0.000	0.797	0.000
Social functioning	0.405	0.016	0.651	0.000	0.741	0.000
School functioning	0.741	0.000	0.838	0.000	0.866	0.000

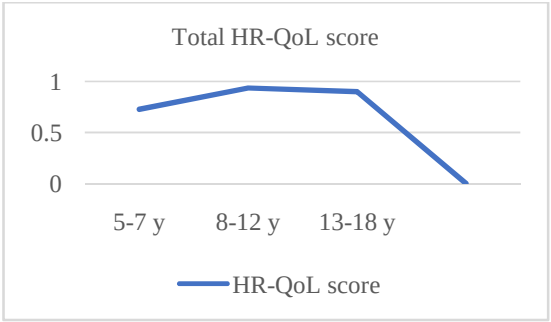

Fig. 1. HR-QoL scores from patient's report.

B. Influencing factors on the HR-QoL of children with HA

The following factors was chosen for analysis: education level, severity, family history, site of bleeding, treatment hospitalization period, and disease duration and the results are given in Table 5.

According to Table 5, it has been shown that children with lower primary level had better HR-QoL than children, studying secondary school from patients' report (65.7 ± 16.8 vs54.6 ± 15.7, p = 0.023) and from parents' report (65.1 ± 15.7 vs 51.7 ± 14.9, p = 0.003).

Table 5: The factors related to total HR-QoL of patients.

	N	Patients' report	P-value	Parents' report	P-value
Education level					
< Primary	29	65.7 (16.8)	0.019	65.1 (15.7)	0.004
Primary	41	59.1 (16.5)		56.9 (17.1)	
Secondary	45	54.6 (15.7)		51.7 (14.9)	
High school	11	52.0 (17.6)		50.4 (16.0)	
Severity of HA					
Severe	51	56.5 (14.4)	0.085	54.3 (14.2)	0.083
Moderate	64	68.1 (17.8)		56.2 (17.6)	
Mild	11	68.7 (17.0)		66.6 (18.9)	
Family history					
Yes	52	55.2 (15.7)	0.055	54.5 (16.3)	0.293
No	74	60.7 (17.0)		57.8 (16.9)	
Site of bleeding					
Joint bleeds	83	56.0 (14.6)	0.034	55.0 (15.5)	0.215
Other bleeds	43	63.0(19.3)		59.0 (18.6)	
Disease duration	126	-0.365	0.000	-0.372	0.000
Treatment hospitalization period	126	0.021	0.816	0.019	0.837

The results are given as mean (SD) and correlation coefficient.

In addition, children with lower primary education also had higher scores than patients in high school (65.1 ± 15.7 vs 50.4 ± 16.0, p = 0.049).

The patients were divided into two groups based on the site of bleeding: joint bleeds and other bleeds. The results revealed that the patients with joint hemorrhage have poorer HR-QoL than patients with other bleeding (56.0 ± 14.6 vs 63.0 ± 19.3, p = 0.034). Comparison of HR-QoL scores by dimensions between two groups is shown in Table 6.

Table 6: HR-QoL scores among patient according to the site of bleeding.

Patients' report	Joint bleeds (N = 83)	Other bleeds (N = 43)	p
Physical health	34.2 (23.4)	45.0 (30.6)	0.005
Psychosocial health	67.2 (16.1)	72.5 (16.3)	0.081
Emotional functioning	56.0 (21.3)	68.5 (22.9)	0.004
Social functioning	85.6 (17.3)	83.1 (19.7)	0.497
School functioning	63.6 (26.7)	66.7 (27.6)	0.533
Total HR-QoL score	56.0 (14.6)	63.0 (19.3)	0.034

The results are given as mean **(**SD**).**

Table 6 shows children with joint bleeds have worse HR-QoL than those with other bleeds on physical health (34.2 ± 23.4 vs 45.0 ± 30.6, p= 0.05) and emotional functioning (56.0 ± 21.3 vs 68.5 ± 22.9, p = 0.004).

Among pediatric participants, it has been found that children with family history have lower HR-QoL scores than children without family history (55.2 ± 15.7 vs. 60.7 ± 17.0, p = 0.055 from patient's report; 54.5 ± 16.3 vs. 57.8 ± 16.9, p = 0.293 from parents' report). This difference was not significant with p > 0.05.

Considering the severity of disease, this study indicated that HR-QoL scores decreased with increase in the severity from mild to severe with 56.5 ± 14.4, 68.1 ± 17.8 and 68.7 ± 17.0 (p=0.085) from patients' report and 54.3 ± 14.2, 56.2 ± 17.6 and 66.6 ± 18.9 (p=0.083) from parent's report. This was not significantly different with p value > 0.05. However, among the patients with severe and moderate HA in age group I, patients' report showed significant impairment in the total HR-QoL score (56.9 ± 15.3 vs 68.8 ± 14.2, p = 0.030) and in physical health (32.9 ± 24.6 vs 52.8 ± 28.5, p = 0.046), whereas from parents' report, children with severe level had lower scores compared to those with moderate level in overall HR-QoL (53.6 ± 14.0 vs68.5 ± 14.1, p = 0.007) and in two dimensions physical health (28.9 ± 24.2 vs 49.7 ± 26.4, p = 0.027), psychosocial health (66.3 ±14.4 vs 78.3 ± 13.0, p = 0.023) and emotional functioning (59.0 ± 17.3 vs 72.2 ± 18.6, p = 0.049). The results are presented in Table 7.

Disease duration showed a statistically significant negative correlation with HR-QoL scores from patients' (r = –0.365, p = 0.000) and parents' report (r = –0.372, p = 0.000). In contrast, there was no statistically significant correlation between HR-QoL and treatment hospitalization period as stated in patient's (r = 0.021, p = 0.816) and parents' report (r = 0.019, p = 0.837).

Table 7: HR-QoL scores among patients with severe and moderate level in age group I.

	Patients' report			Parents' report		
	Severe (N=14)	Moderate (N=18)	P	Severe (N=14)	Moderate (N=18)	p
Physical health	32.9 (24.6)	52.8 (28.5)	0.046	28.9 (24.2)	49.7 (26.4)	0.027
Psychosocial health	69.4 (15.5)	77.3 (15.5)	0.162	66.3 (14.4)	78.3 (13.0)	0.023
Emotional functioning	58.3 (20.7)	69.4 (23.9	0.176	59.0 (17.3)	72.2 (18.6)	0.049
Social functioning	86.7 (18.8)	84.0 (15.6)	0.650	78.3 (22.7)	89.2 (15.7)	0.100
School functioning	66.5 (32.7)	80.3 (20.0)	0.180	63.5 (27.1)	75.2 (18.9)	0.165
Total HR-QoL score	56.9 (15.3)	68.8 (14.2)	0.030	53.6 (14.0)	68.5 (14.1)	0.007

The results are given as mean **(**SD**).**

DISCUSSIONS

HR-QoL is an outcome that is vital for evaluation of HA treatment, so several hemophilia-specific instruments has been recently developed and validated including Hemo-QoL and CHO-KLAT (Bullinger *et al.,* 2002; Young *et al.,* 2006; Remor *et al.,* 2004). However, both of them are not available in Vietnamese. In addition, many studies on linking Hemophilia and HR-QoL have utilized generic HR-QoL instruments such as Peds-QL and the HUI for children [7Poon *et al.,* 2012; Srivastava *et al.,* 2013; Young *et al.,* 2012; Barr *et al.,* 2002). This is the reason why the recent study used Peds-QL questionnaire to access HR-QoL of children and adolescent with HA. Our survey was carried out on 126 males in three age group I (5-7), II (8-12) and III (13-18) with a ratio of 1: 1.17:1.39. The study population of 100% male is in agreement with most studies (Tantawy *et al.,* 2011; Wang *et al.,* 2004; Van der Net, *et al.,* 2006). The reason was that HA is an X-linked disorder that has typical effects on males while the females appear to be carriers. Moreover, the age distribution in this study matches with the survey of WFH in 2015, which reported that Hemophilia A was more common in older children than the younger ones (World Federation of Haemophilia, 2016).

The moderate and severe levels of HA severity was accounted for the major proportion (over 90%) among study sample, which was similar to the study of Taha *et al*., (73.3%). Among the sites of bleeds, manifestations usually occurred in joints and mucous membranes, which were also reported by WFH in 2012.

In general, it has been found that HA had moderate impact on their HR-QoL with total score more than 50 in all age groups, in which, there was more impairment on physical health than psychosocial well-being. This is in agreement with the results of Tantawy *et al.*, in Egypt and Taha *et al*., in Iraq. On the other hand, a study in US reported higher overall HR-QoL scores of HA children (85.9 ± 13.8) with better physical health as compared to psychosocial health (89.5 ± 15.2 vs 84.1 ±15.3) (Poon *et al.,* 2012). This could be explained by the fact that Vietnam is a developing country so there are significant disadvantages in managing Hemophilia patients for instance, lack of health care infrastructure and human resources suitable for hemophilia care, low awareness across the medical profession and non-availability of factor concentrates (Ghosh, 2016). As a result, HR-QoL of patients in this study are poorer.

Besides, it has been shown that among three psychosocial dimensions, social functioning were less impaired than two other functions, the scores of emotional were nearly equal to that of school function from both report of patients and parents in three age groups. Nevertheless, according to the study of Poon *et al.*, in children aged 2-17, social functioning had the highest HR-QoL score (87.7 ± 16.9), followed by emotion and school functioning (82.2 ±19.1 and 81.6 ± 17.3, respectively). The explanation for this contrary is that children in Vietnam with limited understanding of Hemophilia A sometimes tease patients for their disease or do not want to make friends with them, thus, their social relationship is restricted (Poon *et al.*, 2012).

In this study, there was statistically significant difference intotal HR-QoL score between age group I and III from patients' report (64.9 ± 15.7 vs 53.7 ± 15.5, p= 0.006) and from parents' report (64.0 ± 16.5 vs 51.2 ± 14.7, p = 0.001). These findings were opposed to the previous study in Egypt which recorded that age groups had no effect on HR-QoL score (Tantawy *et al.*, 2011). In fact, HA is a chronic disease and children are generally diagnosed with HA in young age. Thus, the older children often have longer disease duration, which can lead to more impairments and problems in their HR-QoL compared to the younger peers.

This paper indicated the impact of site of bleeding on HR-QoL, especially on physical health. This is in accordance with the findings of Ferreira *et al*, (2013). which reported the presence of target joints that was strongly associated with the total score (p < 0.001). This could be explained by the fact that the presence of joint bleeds easily leads to permanent joint damage or the destruction of joint function, in consequence, it causes many disadvantages for children in daily activities.

This study also confirmed the significant difference in HR-QoL between severe and moderate HA patients in age group I.

This is in agreement with the report by Miners *et al.*, who supposed that patients with severe HA generally recorded poorer HR-QoL (Miners *et al.* 1999). Furthermore, researchers reported that the severity of HA negative affected HR-QoL (Poon *et al.,* 2012, Taha and Hassan 2014). This may be related to high morbidity with severe HA. Children with severe level generally had more serious conditions with higher frequency of hospitalization than children with moderate level. In such case, bleeding can lead to life-threatening conditions such as intracranial and gastrointestinal hemorrhages, which reduces HR-QoL in patients.

There are some limitations in this study. Firstly, the study sample consisted of patients treated at Children's Hospital 1 and were aged 5-18 years. Because of this reason, the findings only represented the regional population. Therefore, future studies should include all persons with HA in Vietnam to provide an overview of this disease. Secondly, although Peds-QL questionnaire measured the influence of HA on patients, the use of hemophilia-specific instruments should be considered to provide some particular insight into the HR-QoL of HA patients. Lastly, the study data was collected in 3 months, thus, this study did not record the changes of HR-QoL in HA patients over time. Longer data collection period is recommended.

CONCLUSION

The result of this study indicated that the HR-QoL of children with HA was impaired moderately. Furthermore, education level, age group, disease duration were associated with Peds-QL scores. In addition, site of bleeding was the factor that was relevant to the total scores reported by patients. Therefore, this needs more concerns of care and future studies are necessary in order to improve HR-QoL of HA children.

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