UNIVERSITY of RWANDA

ASSESSMENT OF HEALTH-RELATED QUALITY OF LIFE IN RWANDAN CHILDREN WITH HEMOPHILIA

BY

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DECLARATION

I declare that this Dissertation contains my own work except where specifically acknowledged, and it has been passed through the anti-plagiarism system and found to be compliant and this is the approved final version of the thesis.

Jean Claude NTIYAMIRA, Reg no: 10106517

Signature.....

Date: August ,2020

Dr Aimable KANYAMUHUNGA

Signature .....

Date: August,2020

DEDICATION

To almighty God who guides us

To my mother FRANCINE MUKABADEGE whose unconditional love, prayers and daily encouragement helped me so much in this work

To my other family members and relatives

I dedicate this work

AKNOWLEDGEMENT

This work would not have been achieved without support of many benefactors. We wish to thank all of those, close or far, who contributed to the realization of this work.

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To all of you, we say thanks a lot

ABSTRACT

Background:

Hemophilia, a rare congenital chronic bleeding disease, the management of which poses major challenges, mainly in developing countries, may have a more serious impact on the quality of life (QoL) of the Rwandan hemophilia population. This research mainly assessed the QOL of children with hemophilia and their parents using Hemo-Qol questionnaire and identified important contributing factors of QOL.

Methods:

It was a cross-sectional study, consisting of 27 children in total with 11 children ≤ 7 years as group I, 8 children of 8-12-years-old, and 13-16 years as groups II and III respectively along with their 23 parents followed in hematology clinic OPD/CHUK in 2019. The recruitment of the participants was done by telephone call during the study period in order to attend the clinic on their specific allocated time. The Hemo-Qol questionnaire was used to assess the quality of life after translation into Kinyarwanda. This is a Liquert scale with a maximum score of 5 in each area tested. Totals are calculated from the individual domains and then an overall score is found; then the percentage transformation was performed with a high score indicating a poorer quality of life. Data were analyzed in SPSS using Student's t-test for statistical analysis.

Results:

The total mean Haemo-QoL scores were 43.7 ± 14.8 and 46.3 ± 14.3, respectively, for children and their parents. Children between 8 and 12 years old are mainly affected in the areas of feeling (67 ± 29.6) and adolescents in the future (70.3 ± 6.5). Treatment (54.5 ± 39.2) in young children ≤ 7 years, feeling (71 ± 18.3) in 8 to 12 years and family (62.5± 9.7) in adolescents, were the main areas of altered quality of life reported by parents.

The only significant differences when comparing health related quality of life (HRQL) as children's reports and HRQL as parental reports were observed between children of group III and their parents in the field of sport and school (score of 45.8 ± 2.6 among parents and the score of 40.6 ± 21.8 in children, with a P value <0.05).

Among children aged 8 to 12 year, those who missed school one or more times in the month before the study have significant deterioration in various dimensions of Qol, including feelings, family, other person, and treatment relative to children who have not missed school with a P value <0.05.

Adolescents with severe hemophilia scored high with 52.1 of total score among friends of the subscale compared to those of moderate type 22.1 with P value <0.05, similar to those who bleed more than once with a significant deterioration in the future of the subscale with 73.8 vs 64.6 with those who did not have a bleeding episode; P = 0.05.

Rural residence with young age for children with severe hemophilia; age 8-12 with parents with public insurance (CBHI) were negative factors in differents area of QOL.

Conclusions:

The QOL was insufficient in the Rwandan pediatric hemophilia population. The feeling and future subscales in children and the treatment, feeling and family subscales in parents were the main areas of impaired QOL in our study. This study also showed that children who miss school have a reduced QOL in addition to those with severe hemophilia, frequent bleeding episodes, long distance to the hemophilia treatment center and those whose parents use public insurance(CBHI).

Emphasis should be placed on efforts to improve integrated care strategies for hemophilia: focused on medical care with advocacy for the use of prophylaxis and psychosocial education for parents and children with haemophilia.

KEY WORDS:

Assessment

Quality of life

Hemophilia

Children

Rwanda

LIST OF SYMBOLS AND ACRONYMS

CBHI: community based health insurance

CEM: centre excellence mpore

CMHS: college of medicine and health sciences

CHUB: centre hospitalier universitaire de butare (university teaching hospital of butare)

CHUK: centre hospitalier universitaire de kigali (university teaching hospital of kigali)

HRQL: health-related quality of life

IRB: institutional review board

MOH: ministry of health

OPD: outpatient department

PI: primary investigator

PRO: patient reported outcome

PWH: patient with hemophilia

QoL: quality of life

RFH: Rwanda fraternity against hemophilia

RS: raw score

SSS: standardized scaled scale

SPSS: statistical package for social science

TSS: transformed scared score

UR: university of Rwanda

VWD: von Willebrand disease

WFH: world federation of hemophilia

TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

CHAPTER ONE: INTRODUCTION

BACKGROUND

Hemophilia is a rare chronic congenital bleeding disorder due to a deficiency of coagulation factors VIII (hemophilia A) and IX (hemophilia B)(1). Persons with haemophilia (PWH) are at risk of bleeding for the course of their lives, with or without trauma depending on clotting factor level, and their treatment requires replacing the missing factor, either therapeutically or prophylactically (2).

The global incidence of hemophilia A is estimated at 1 / 5,000 newborns, while B occurs in approximately 1 in 30,000, with variations in the reported prevalence of hemophilia worldwide (3).

Chronic hemarthrosis causes synovial enlargement and cartilage damage, with progressive destruction of the joints leading to hemophiliac arthropathy (4). This can lead to lifelong disability and a significant deterioration in the QOL of patients with hemophilia (5).

In addition to this effect on physical health, hemophilia population suffer a significant negative psychological, social and financial impact. Shapiro and colleagues study found that hemophiliac children may not reach their full potential at school and later in life due to a higher frequency of school absenteeism and bleeding episodes (6). Other researches have shown that hemophiliac children have emotional and behavioral difficulties compared to healthy children (7). Quality of life studies have emerged as an important method of evaluating the medical care received by hemophiliac patients (8).

QOL is a concept that assesses the general well-being of a patient. It is too broad a concept to assess the effectiveness of medical care in hemophilia, as it involves an assessment of health and non-health aspects of life. In this document, we will focus on health-related quality of life (HRQL).

HRQL is a person's subjective perception of the disease and its treatment on physical, psychological (emotional, mental, social and behavioral) and social functioning. It is a subjective experience, which means that only patients and / or observers can inform providers of their views and experiences related to the disease.

Conceptually, HRQL pediatric studies are designed to assess a wider range of children's daily functioning than clinical measures, and their results provide unique information beyond clinical symptoms (9).

The QoL of children with other conditions, such as asthma and leukemia, is increasingly studied compared to that of young hemophiliac patients (10).Understanding the QOL of hemophilia population is important to improve the medical care they receive (8).Measuring HRQL on a quantifiable basis using a specific measurement tool can be beneficial as it can identify patients at risk for problems related to hemophilia (11),this information can help decision-making by doctors and patients, and can help develop strategies for adequate allocation of resources and management-related health policies (10).

No pediatric hemophilia related study has been conducted in Rwanda and very little information is available only in the newspapers. CHUK is one of the referral hospitals in the capital of Kigali, Rwanda, and receives patients who are transferred from district hospitals in different provinces. It has many departments, including the pediatrics department, which has many pediatricians, residents, general practitioners and nurses to care for all sick children, including children with hemophilia.

Children with hemophilia are followed in the outpatient department (OPD) at the centre excellence mpore (CEM) and some are seen in pediatric emergency when they have bleeding problems. There is only one pediatric hemato-oncologist in Rwanda who tracks these hemophiliacs children, and CHUK is the only center where factor replacement therapy is accessible through donations from support groups, including the World Federation of hemophilia (WFH) since 2012.

Currently, hemophilia management is growing, including factor replacement prescriptions, as well as the availability of group association (RFH). This study would help us to understand the level of hemophilia care in our communities and to implement the appropriate interventions.

PROBLEM STATEMENT

Children with hemophilia suffer from complications related to bleeding symptoms, according to the level of missing clothing factor , classified as mild, moderate and severe(12). The impact on QOL may depend on the frequency and severity of the bleeding and its management(13). This good management depends on how quickly the appropriate dose of the

deficient factor is replaced in response to injury or bleeding(2). This bleeding can be prevented by prophylaxis, but this type of management is difficult and expensive and requires the development of a support infrastructure. The care these patients need is better provided in hemophilia treatment centers (HTCs). They are dedicated centers of excellence with multidisciplinary resources and a capacity for lifelong care and monitoring of patients with hemophilia which is not yet established at CHUK and none is available throughout the country. There is only one pediatric hematologist available to monitor all of these patients, no nurse responsible for coordinating hemophilia care activities, no social worker to help resolve insurance and transportation issues of hemophiliac patients, no physiotherapist and orthopedist to help in hemophilia care at the CHUK hematology clinic. This explains the level of care for hemophilia in our communities, which has a significant impact on the QOL of hemophiliac population.

To our knowledge, there are no published articles on hemophilia in Rwanda and this is the first study assessing the HRQL in children with hemophilia and their parents with the need to better understand the effectiveness of care received by hemophiliac children in Rwanda.

GENERAL STUDY OBJECTIVES

Evaluate the QOL of children living with hemophilia and their parents using the Hemo-Qol questionnaire and identify the important factors that contribute to QOL.

SPECIFIC OBJECTIVES

1. To determine the overall QOL of Rwandan children living with hemophilia as reported by the affected children and their parents.
2. Compare the Children's reports to Parents' reports HRQOL.
3. To correlate demographic data and HRQL reported by hemophilia respondents.

CHAPTER TWO: LITERATURE REVIEW

Hemophilia is a congenital, chronic bleeding disorder due to a lack of coagulation factors VIII (Hemophilia A) and IX (Hemophilia B)(1). It is mild, moderate, or severe depending on the level of missing clothing factor and the number of bleeds. Muscle and joint bleeding are the main concern of hemophilic patients, with gradual joint destruction, later to hemophilic arthropathy, if not treated properly, leading to a serious impairement in the QOL(4,5,12).

From a research perspective, replacement of the missing factors and many advances in the treatment of hemophilia have greatly contributed to better care and a substantial improvement in the QOL for PWH (14). Early prophylactic therapy in patients with severe hemophilia shown to reduce musculoskeletal deterioration and improve QOL by enabling their better life and physical development (15). Qol studies have proven to be an important tool in assessing the health of PWH (16).

A Colombian study found HR-QOL as high in hemophiliac patients as in the general population, while almost all (96.6%) of hemophiliac patients were on prophylaxis(17).

A 3-month-long study in China showed improvement in bleeding complications in children living with hemophilia by comparing the prophylaxis and on-demand treatment phases with a significant relative improvement in QOL for their parents(18).

The management of hemophilia is a major challenge in developing countries, like the study by Ghosh et al, including many contributing factors: inadequate health infrastructure and health personnel for hemophilia care, lack of health insurance, less priotisatization of hemophilia patients in the healthcare system, no availability of the factor concentrates and no available specific research on hemophilia(19).

The positive or negative predictive factors that affect the QOL of PWH differ from country to country not only related to the health characteristics of the disease (severity of hemophilia, number of bleeds, development of inhibitors, etc.) and treatment of the disease (prophylactic versus on demand) at the national level, but also psychosocial factors, explained by the social support they receive and their satisfaction with life(20).

Studies have shown that patients with mild and moderate hemophilia experience more treatment difficulties due to a likely insufficiency knowledge and experience with the symptoms of the disease and a weak capacity for self-care; while anxiety or depression are the main contributors to treatment difficulties in patients with severe hemophilia(21).

According to Tantawy et al, Egyptian children with hemophilia A (one third of whom were on prophylaxis) experienced an important deterioration in QOL with total scores greater than 50 on all subscales; in children aged 4 to 7, the dimension of greatest disability was in the treatment subscale, while the dimensions of physical health were greatly affected in the age groups 8 to 12 and 13 to 16 years old (22).

Bagheri et al. in Shiraz, Iran, they studied QOL in a consensus sample of 27 male children with hemophilia and their parents. None of the patients were on prophylaxis,60% of the parents declared an adequate income and many mothers had a basic education level. The study showed a significantly deteriorated QOL with a total average score of 54.1 ± 7.3 with impaired friends and perceived support subscales in the 8-12 and 13-16 age groups; Family income and parental administration of the product were factors that predicted poor quality of life in these children (23).

In a study in India, the QOL was uniformly worse among affected children and their parents (score range 42.2 ± 8.5 to 45.0 ± 9.5) with a perceived impact on the family, physical health and school / sports which have greatly contributed to a worse quality of life (24).

In Basra, Iraq, the family dimension was most affected among young children. The ability to play sports was affected in children 8 to 12 years of age. Among adolescents, the largest dimension of impairment was perceived support. The severity of hemophilia and> 5 bleeds per year significantly affected the total QOL score (8).

HR-QOL assessment by Dis et al.in Filipino children, showed a total average score of 28.39 ± 4.76, reflecting the good quality of life of Filipino children compared to children of Turkey, Egypt and Iran with an overall average score of 39.6 ± 15.0, ≥ 50 and 54.1 ± 7.3 respectively(22,23,25). In Filipino children; the family subscale was the dimension most affected in young children, explained by parents over-protecting them, while children aged 8 to 12 and 13 to 16 had the greatest disability in the Sports and School subscale. Parents' scores reflected similar areas of greater disability than their children(26).

CHAPTER THREE: MATERIALS AND METHODS

TYPE OF STUDY

This is a descriptive cross sectional study design

STUDY POPULATION

All children diagnosed with hemophilia A or B and their parents followed up at the CHUK in the Department of Pediatrics under the study period (2019).

Inclusion criteria

- Children 8 to 16 years old diagnosed with hemophilia A or B
- All parents of children with hemophilia, regardless of children age, followed at the hematology clinic.
- Children whose parents signed the consent form

Exclusion criteria

- Subjects with different comorbidities (congenital, chromosomal or neurological abnormalities) and those with certain systemic diseases (such as diabetes, cardiovascular disease, chronic kidney disease), as these disorders may have their own quality of life burden which can bias the results.
- Children whose parents did not sign the consent form

STUDY SITE

This study has been conducted in the Department of Pediatrics at CHUK.

CHUK is a tertiary level hospital located in Kigali City, Rwanda. The CHUK is one of the three main national public referral hospitals: CHUK, CHUB and the Rwandan military hospital. It mainly receives patients transferred from district hospitals, in particular patients requiring a specialist consultation. The Pediatrics Department is composed of neonatology unit and pediatric wards having cardiology, oncology units, general ward, chronic ward and surgical ward. It has also a Pediatric High Dependent and Intensive Care Unit and Emergency Unit which receives acutely-ill patients. It has also an outpatient unit which has three parts: the section for follow-up of children living with HIV/AIDS, general pediatrics section (which receives all children with various diseases from district hospitals, home and private clinics), and a subspecialty section mainly hematology, oncology, pulmonology, genetic, cardiology

and nephrology. Regular follow-up of children with hemophilia is done in hematology clinic once a week.

There is only one pediatrician hemato-oncologist in Rwanda, therefore, all children with hemophilia are followed and receive their treatment at CHUK as a comprehensive hemophilia treatment center site in Rwanda. Therefore, this study is likely to capture the entire population of known pediatric patients with hemophilia in the countrywide.

DATA COLLECTION PROCEDURES:

Study instruments

A special designed questionnaire and medical information from patients using the CHUK open clinic were used to collect information on demographic and clinical characteristics. The quality of life was assessed with the Haemo-QoL questionnaire.

The Haemo-QoL questionnaire is a set of questions specific to age and disease to measure the QoL of PWH and their parents developed by Von Mackensen et al with accepted psychometric properties(27–29). There are three versions for three age groups of children and a proxy parent: version I for young children (4 to 7 years: 21 items), II (8 to 12 years: 64 items) and III (13 to 16 years: 77 items) for older children. Haemo-QoL questionnaires cover various areas of QoL, including the physical scale (pain and mobility issues), feelings (mood and emotional consequences of illness); family scale (restrictions on activities and problems at home); friends scale (relationship and activities of the child with his friends); perceived support scale (how children recognize the social support and isolation they receive from others); sports and school (sports participation and school activities), treatment scale (hemophilia care and side effects of treatment); other people (how the patient interacts with others); future and relationships (children's views of the future and the possibility of having relationships with the opposite sex in adolescents).

Translation methods of the questionnaire

The original questionnaire in English was provided by Dr. Sylvia von Mackensen (developer) who gave us permission to translate it for this study. This original English questionnaire was translated into Kinyarwanda by a bilingual professional translator and submitted to experts for evaluation, composed of two specialists in hematology (pediatric and adult). The suggestions made by the two doctors were incorporated into the Kinyarwanda translation, then the questionnaire was retranslated into English by a second translator without much disagreement.

Patient recruitment

Case recruitment and collection of certain demographic / clinical data was done by examining the medical information of patients at the CHUK Open Clinic to identify those who meet the inclusion criteria and their address; We proceeded with calling the parents in order to attend the clinic on their specific allocated time. A total of 27 children have been recruited with 11 children ≤ 7 years old in group I, 8 children of 8-12 years, and 13-16 years old in groups II and III, respectively along with their 23 parents followed in hematology clinic OPD/CHUK in 2019 were included as well in the study.

Data collection

After obtaining informed consent from parents, the primary investigator(PI) distributed questionnaires to children and their parents responsibly.

The following information was obtained from parents using a designed clinical demographic questionnaire: age of parents and children, sex of caregiver, residence, relationship with guardians, social category or Ubudehe which is a revised categorization of Rwandan households into 4 categories (6 previous) of socio-economic status according to household income and living conditions(30), type of insurance , level of education of the caregiver, profession of caregiver, type of hemophilia, severity of the disease, type of treatment (on demand or prophylaxis), type of product received when bleeding occurred, number of bleeds , school absenteeism and bleeding site a month before the study .

The Kinyarwanda Hemo-Qol questionnaire was administered to children and their parents; divided into 2 age groups for the child version questionnaire: group II (8 to 12 years old) and group III (13 to 16 years old) while 3 age groups for the parent's version questionnaire : group I parents of children from 0 to 7 years old, group II parents of children from 8 to 12 years old and group III parents of children from 13 to 16 years old according to the age group of the Hemo-Quality of life questionnaire. This is a Liquert scale with a maximum score of 5 in each area tested. Totals are calculated from the individual domains, then an overall score is found; then the percentage transformation is performed with a high score indicating a lower QOL.

DATA-MANAGEMENT

Information from these two sources, including demographic / clinical questionnaires and Hemo-Qol, was entered in the Social Sciences Social Package (SPSS) version 25.0 which we used in cleaning, editing and post-processing datas.

STATISTICAL ANALYSIS

Haemo-QoL scores were available after qualifying the questionnaire as the hemo-Qol group manual provided on the website http://www.haemoqol.de, assigning a number to the response scale, which were for both the children and the parents responses: 1 = never, 2=seldom, 3 = sometimes, 4 = often and 5 = all the time in our study. The sum of the items that belong to each subscale produces the raw score (RS) by subscale. The range was between the lowest possible (number of items (n) x 1) and the highest possible (number of items (n) x 5 in children and parents. The scores on the subscales were compared; this raw score divided by the number of items on the scale, the resulting standard scale (SSS) score can have any value (also decimal) between 1 and 5. A value of 1 represents the highest possible quality of life score and a value of 5 the lowest possible quality of life score: the transfer from a raw score to a transformed scale score (TSS) between 0 and 100 allowed express the scale score as a percentage between the lowest value (0) and the highest (100), for example if 1= never, then 20% would be the lowest possible score. Most important that the higher the score, the worse the QOL.

The data was analyzed with version SPSS 25.0 and presented in the form of tables and graphs, if available mean and standard deviation for the quantitative variables, the frequencies and the proportion for the categorical variables were carried out for the descriptive analysis. The comparison between the HRQoL child's reports and the parents' reports was evaluated by comparing the mean values using the paired t-test and the correlation of the demographic / clinical characteristics with the HRQoL reported by the child and the parents were evaluated using the independent t-test. Any difference with the P value <0.05 was considered statistically significant.

ETHICAL CONSIDERATIONS

This research proposal was submitted to the IRB of the CMHS ethics committee for review and approval. It was also approved by the CHUK research and ethics committee. The purpose of this study and its importance were explained to caregivers before deciding to be included in the study. This study was conducted in accordance with the principles of the Helsinki Declaration and good clinical practice. In addition, enrollment in the study was based on consent given to parents. All the data was stored in the pediatric ward in a locked drawer.

REFERENCES MANAGEMENT

Our references were managed by Mendeley software in the style of Vancouver.

CHAPTER FOUR: RESULTS

DEMOGRAPHIC AND CLINICAL CHARACTERISTICS

TABLE 1A: AGE AND TYPE OF HEMOPHILIA.

		Type of hemophilia	
		A	**B**
Age of the child	0-7 years (n=11)	8 (72.7%)	3 (27.3%)
	8-12 years (n=8)	5 (62.5%)	3 (37.5%)
	13-16 years (n=8)	6 (75%)	2 (25%)
Total (n=27)		19 (70.4%)	8 (29.6%)

TABLE 1B: DEMOGRAPHIC AND CLINICAL CHARACTERISTICS OF HEMOPHILIAC RESPONDENTS

		Count	**%**
Age of parents	18-45	14	60.8
	45-55	7	30.4
	>55	2	8.6
Residence	urban (kigali)	13	56.5
	RURAL (PROVINCE)	10	43.4
Relationship with the patient	Mother	14	60.9
	Father	6	26.1
	Other	3	13
Insurance	Community-based health insurance (CBHI)	19	82.6
	Other insurance	4	17.4
Wealth index (ubudehe)	1&2	15	65.2
	3&4	8	34.8
Level of education for the parents	None	2	8.7
	Primary	9	39.1
	Secondary	8	34.8
	University	4	17.4

Severity of hemophilia	Mild	5	18.5
	Moderate	8	29.6
	Severe	14	51.9
Type of treatment	On demand	26	96.3
	Prophylaxis	1	3.7
Medication given in the last 4 weeks	FFP or Cryoprecipitate	8	29.6
	Factor VIII or IX	9	33.3
	None	10	37.1
Number of bleeding episodes in the last 4 weeks	None	10	37
	1-5 times per month	16	59.3
	>5x per month	1	3.7
Number of joints bleeding in the last 4 weeks	one site	4	14.8
	More than 1	17	63
	None	6	22.2
Number of school absences	None	4	17.4
	once a month	6	26.1
	> once a month	13	56.5

The 23 parents completed the questionnaires on demographic and clinical characteristics and the Hemo-Qol parents' questionnaire corresponding to their children's age groups, three of them completed more than one questionnaire for their children, namely a total of 27 parent proxy hemo-Qol responses. The 16 older children, 8 children in group II (8-12) and 8 children in group III (13-16) were able to complete the hemo-Qol questionnaires administered with questions corresponding to their age group.

Seventy percent (70%) (19/27) of respondents have hemophilia A (table 1A), 52% (14/27) of children have severe hemophilia, with all children on demand therapy (receive factor only if bleeding) as a treatment option, except for one child (3.7%) whom the hematologist decided to undergo prophylaxis due to frequent episodes of bleeding. Sixty-three percent (63%) of the children bleed one or more times in the last 4 weeks and many of them (77.8 of those who bleed) declared having bled at least in their joint.

In those who had bleeding, only 53% (9/17) were able to receive factor (VIII or IX) as a prescription drug and 47% (8/17) received plasma derivatives (FFP or cryoprecipitate) (table 1B).

A large percentage (82%) of parents report that their children have missed school at least once a month prior to the study date. Many of the respondents were mothers (60.9%), with an age ≤ 45 years representing 60.8%. Most of the respondents came from urban city of Kigali representing (56.5%) and many of parents use the community-based health insurance (CBHI) (82.6%) (table 1B).

The education levels of most caregivers were primary (39.1%) and secondary (34.8%), including 4 parents (17.4%) who attended university level and 2 parents who had no formal education. Sixty-five percent (65%) of the families are classified in low socio-economic level (Ubudehe category 1 and 2 (table 1B).

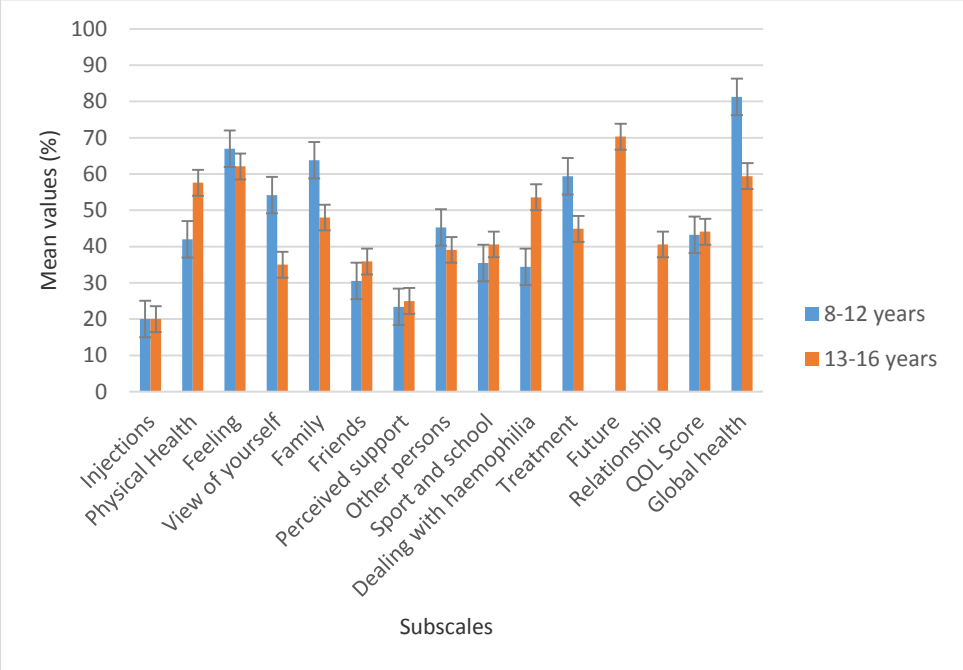

FIGURE 1. HAEMO-QOL SCORES IN DIFFERENTS SUBSCALES AMONG GROUP II AND III CHILDREN

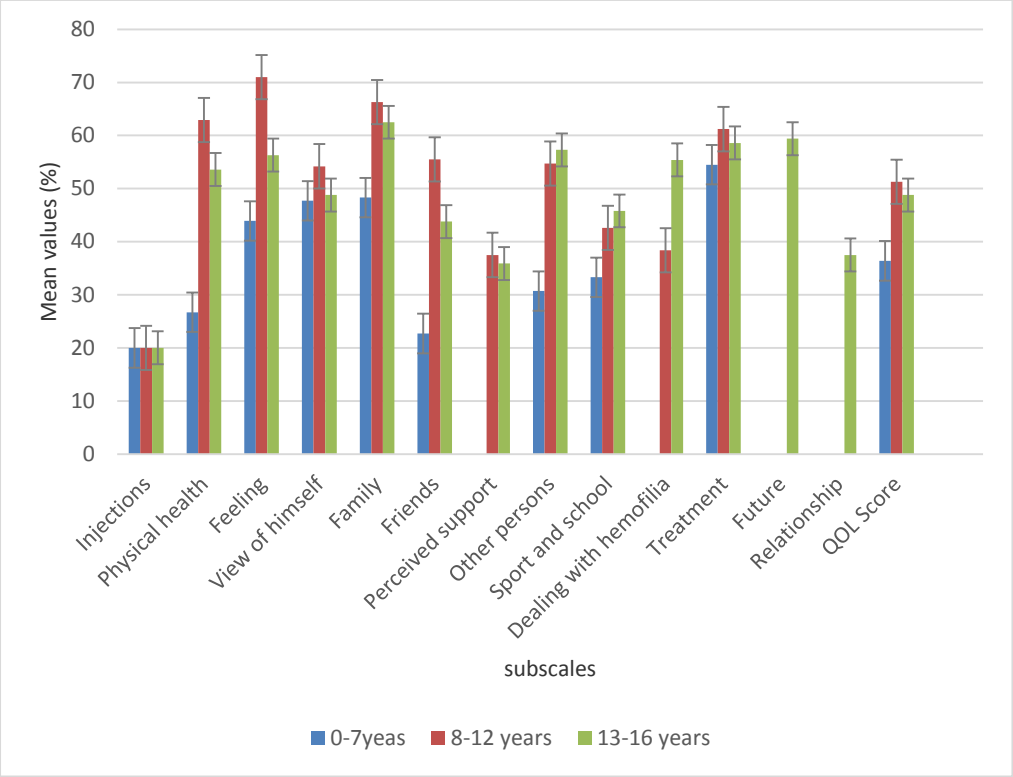

FIGURE 2. HAEMO-QOL SCORES IN DIFFERENTS SUBSCALES AS PARENT PROXY-REPORT FOR THEIR CHILDREN

The mean TSS of all subscale scores for children 8 to 12 years of age and 13 to 16 years of age was 43.2 ± 16.2 and 44.1 ± 14.3 respectively, with an average mean score for children of **43.7 ± 14.8**. It was 36.4 ± 12.5 among parents of children ≤ 7 years old, 51.3 ± 15.2 among parents of children aged 8 to 12 and 48.8 ± 12.1 among parents of 13 to 16 years old, with an overall average score of parents of **46.3 ± 14.3,** indicating a great impairement in the quality of life of parents than of their children (figure 1&2).

Among children, the most deteriorated aspects of life were the feelings subscale (67 ± 29.6) in the 8 to 12 years' age group and the future subscale (70.3 ± 6, 5) in the ages 13 to 16 years (figure 1). Treatment (54.5 ± 39.2) in young children ≤ 7 years' group, feeling (71 ± 18.3) in 8 and 12 years of age and family subscales in 13 to 16 years of age group were the most impaired aspects of quality of life among parents (figure 2). The injection subscale in general obtained a low score (20 ± 0) in children and parents, showing a positive impact on quality of life (Figures 1 and 2). The only significant differences when comparing HRQL as children's reports and HRQL as parental reports were observed between children of group III and their

parents in the field of sport and school (score of 45.8 ± 2.6 according to the parents and the score of 40.6 ± 21.8 in children, with a P value <0.05), indicating parents' great concern as for the participation in sports and school activities of their old children (Table 2)

TABLE 2: COMPARISON OF HRQL AS REPORTS OF CHILDREN AND REPORTS OF THEIR PARENTS.

	8-12 years			13-16 years		
	Parents	**Kids**	**p-value**	**Parents**	**Kids**	**p-value**
Injections	20±0	20±0	>0.999	20±0	20±0	>0.999
Physical health	62.9±21.2	42±27.5	0.382	53.6±21.9	57.6±29	0.206
Feeling	71±18.3	67±29.6	0.733	56.3±11.1	62.1±33.8	0.993
View of himself	54.2±19.5	54.2±9.3	0.602	48.8±6.9	35±17.8	0.682
Family	66.3±7.9	63.8±18.3	0.255	62.5±9.7	48±23.6	0.532
Friends	55.5±28.2	30.5±32.3	0.528	43.8±28.3	35.9±31.3	0.275
Perceived support	37.5±33.4	23.4±27.9	0.67	35.9±16.6	25±23.9	0.297
Other persons	54.7±19.6	45.3±18.8	0.61	57.3±21.2	39.1±22	0.079
Sport and school	42.6±13.9	35.5±17.1	0.343	45.8±2.6	40.6±21.8	**0.018**
Dealing with hemophilia	38.4±12.5	34.4±19.6	0.373	55.4±13.6	53.6±35.6	0.75
Treatment	61.2±18.5	59.4±13.9	0.197	58.6±10.9	44.9±22.3	0.468
Future	-	-	-	59.4±11.1	70.3±6.5	0.341
Relationship	-	-	-	37.5±40.1	40.6±31.9	0.073
Mean	51.3±15.2	43.2±16.2	0.615	48.8±12	44.1±14.3	0.054

Paired t-test analysis

Among children aged 8 to 12, those who missed school one or more times in the past month have also significant deterioration in various dimensions, including feelings, family, another person, and treatment compared to children who have not missed school, P <0.05. (Table 3a).

Adolescents with severe hemophilia scored significantly higher among friends' subscale with a score of 52.1 compared to those with moderate disease with a score of 22.1, p = 0.022, and adolescents who bleed more than once in the past month were significantly impaired in the future subscale with a score of 73.8 versus 64.6 with those who had no bleeding episode; P = 0.038 (Table 4a).

The correlation between HRQL and demographic / clinical characteristics in the parent reporting group I showed a significant deterioration in physical health subscale among young children in rural areas with a score of 45.3 versus 11.3 score in children from the city of Kigali; P = 0.006 and impaired family subscale with a score of 70.3 among young children with severe hemophilia compared to those with moderate disease with a score of 37.5; P = 0.048 (Table 5). Correlation in Parent Report Group II, children of parents who use CBHI insurance (Mituelle de Santé) obtained high scores in other people subscale with a score of 62.5 vs 16.7 in those with other insurances, P = 0.020 and treatment subscales with a score of 69.0 VS 21.4 among other insured, P = 0.004 (Table 3b). The correlations between HRQL in parents respondent group III and the demographic / clinical characteristics did not show any significant differences (Table 4b).

TABLE 3A: DEMOGRAPHIC DATA AND HRQL CORRELATION – CHILD REPORT GROUP II

		Physical Health	Feeling	View of yourself	Family	Friends	Perceived support	Other persons	Sport and school	hemophilia	Treatment
Severity of hemophilia	Moderate	-	-	-	-	-	-	-	-	-	-
	Severe	48.0	66.8	54.8	63.6	34.8	26.8	42.9	38.4	36.7	58.7
	P	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Type of hemophilia	A	34.3	71.4	54.4	68.0	35.0	32.5	52.5	31.3	30.7	63.6
	B	54.8	59.5	53.7	56.7	22.9	8.3	33.3	42.7	40.5	52.4
	P	0.34	0.62	0.92	0.43	0.64	0.26	0.18	0.40	0.53	0.30
Bleeding episodes	None	34.5	50.0	57.4	53.3	16.7	4.2	36.1	39.6	32.1	52.4
	≥ once per month	46.4	77.1	52.2	70.0	38.8	35.0	50.8	33.1	35.7	63.6
	P	0.59	0.23	0.48	0.23	0.39	0.13	0.32	0.64	0.82	0.30
Joint bleeding	None	NA	67.9	50.0	65.0	NA	NA	62.5	15.6	17.9	64.3
	≥ one joint	48.0	66.8	54.8	63.6	34.8	26.8	42.9	38.4	36.7	58.7
	P	NA	0.97	0.66	0.9	NA	NA	0.3	0.2	0.4	0.7
school absenteeism	None	46.4	7.1	52.8	20.0	0.0	12.5	4.2	37.5	10.7	28.6
	≥ once missing school	48.2	76.8	55.1	70.8	40.6	29.2	49.3	38.5	41.1	63.7
	P	0.95	**0.02**	0.850	**0.00**	NA	0.63	**0.00**	0.95	0.17	**0.00**

Student t-test

TABLE 3B: DEMOGRAPHIC DATA AND HRQL CORRELATION – PARENT REPORT GROUP II

		health	Feeling	himself	Family	Friends	support	persons	school	hemophilia	Treatment
Residence	Urban	53.6	61.6	43.1	65.0	40.6	25.0	58.3	38.3	37.5	58.9
	Rural	70.2	78.6	63.9	66.7	66.7	43.8	52.8	46.9	42.9	66.7
	P	0.3	0.26	0.19	0.82	0.26	0.51	0.76	0.50	0.62	0.65
Wealth index	Ubudehe category 1&2	59.8	78.6	62.5	66.3	67.2	50.0	60.4	46.1	42.9	65.2
	Ubudehe category 2&3	67.9	62.5	37.5	65.0	31.3	0.0	66.7	32.8	39.3	76.8
	P	0.73	0.29	0.19	0.89	0.17	NA	0.62	0.40	0.78	0.12
Insurance	CBHI	62.5	73.2	54.2	65.8	55.2	33.3	62.5	41.7	41.7	69.0
	Others insurance	50.0	42.9	38.9	65.0	31.3	31.3	16.7	43.8	28.6	21.4
	P	0.64	0.14	0.53	0.93	0.48	0.96	**0.02**	0.91	0.39	**0.00**

Student t-test

TABLE 4A DEMOGRAPHIC DATA AND HRQL CORRELATION – CHILD REPORT GROUP III

		Physical Health	Feeling	View of yourself	Family	Friends	Perceived support	Other persons	Sport and school	Dealing with hemophilia	Treatment	Future	Relationship
Severity	Moderate	32.1	58.3	27.5	38.5	22.1	0.0	31.9	21.3	19.0	39.6	66.7	41.7
	Severe	65.5	66.7	38.3	56.3	52.1	35.4	52.8	56.5	69.0	51.0	72.9	37.5
	P	0.14	0.81	0.58	0.48	**0.02**	NA	0.33	0.07	0.08	0.63	0.34	0.89
Type of hemophilia	A	51.2	52.1	30.0	44.8	38.5	26.0	43.8	41.7	49.4	40.6	68.8	33.3
	B	76.8	92.2	50.0	57.8	28.1	21.9	25.0	37.5	66.1	57.8	75.0	62.5
	P	0.31	0.15	0.18	0.54	0.71	0.84	0.33	0.83	0.60	0.38	0.26	0.29
Bleeding episodes	None	60.7	50.0	35.8	53.1	47.9	33.3	48.6	40.7	59.5	40.6	64.6	33.3
	≥ once per month	55.7	69.4	34.5	45.0	28.8	20.0	33.3	40.6	50.0	47.5	73.8	45.0
	P	0.83	0.47	0.92	0.67	0.44	0.48	0.38	0.99	0.74	0.70	**0.03**	0.65
Joints bleeding	None	71.4	37.5	42.5	59.4	68.8	50.0	41.7	41.7	89.3	31.3	68.8	12.5
	≥ one joint	55.6	65.6	33.9	46.4	31.3	21.4	38.7	40.5	48.5	46.9	70.5	44.6
	P	0.64	0.47	0.68	0.64	0.29	0.29	0.91	0.96	0.31	0.55	0.81	0.38
school absenteeism	None	48.8	62.5	32.9	47.4	27.1	17.7	42.4	38.9	44.0	45.3	69.8	39.6
	≥ once missing school	96.4	84.4	40.0	40.6	56.3	43.8	16.7	50.0	75.0	56.3	75.0	75.0
	P	0.16	0.60	0.76	0.82	0.42	0.34	0.36	0.70	0.46	0.70	0.53	0.35

Student t-test

TABLE 4B. DEMOGRAPHIC DATA AND HRQL CORRELATION – PARENT REPORT GROUP III.

		health	**Feeling**	**himself**	**Family**	**Friends**	**support**	**persons**	**school**	**hemophilia**	**Treatment**	**Future**	**Relationship**
Residence	Urban	48.2	59.4	48.8	63.3	34.4	31.3	66.7	45.8	48.2	64.8	56.3	56.3
	Rural	54.8	55.2	47.5	63.5	47.9	37.5	51.4	45.4	60.7	53.1	60.4	16.7
	P	0.73	0.67	0.84	0.97	0.5	0.67	0.3	0.84	0.26	0.19	0.67	0.26
Wealth index	Ubudehe category 1&2	47.6	59.4	47.5	64.6	35.4	31.3	63.9	45.4	51.2	61.5	56.3	41.7
	Ubudehe category 2&3	53.6	56.3	48.8	62.5	43.8	35.9	57.3	45.8	55.4	58.6	59.4	37.5
	P	0.76	0.75	0.84	0.81	0.7	0.75	0.7	0.84	0.72	0.77	0.75	0.91
Insurance	CBHI	42.9	61.9	46.5	66.3	28.8	27.5	69.2	45.0	47.9	63.8	53.8	45.0
	Other insurance	71.4	46.9	52.5	56.3	68.	50.0	37.5	47.2	67.9	50.0	68.8	25.0
	P	0.13	0.11	0.37	0.27	0.09	0.11	0.06	0.37	0.07	0.15	0.11	0.62

Student t-test

TABLE 5: DEMOGRAPHIC DATA AND HRQL CORRELATION – PARENT REPORT GROUP I.

		Physical health	Feeling	View of himself	Family	Friends	Other persons	Sport and school	Treatment
Residence	Urban	11.3	40.0	35.0	56.3	10.0	20.0	21.7	65.0
	Rural	45.3	56.3	53.1	46.9	50.0	56.3	37.5	59.4
	P	**0.006**	0.360	0.542	0.621	0.076	0.220	0.474	0.842
Wealth index	Ubudehe category 1&2	24.2	46.9	48.4	50.8	25.0	34.4	32.3	67.2
	Ubudehe category 2&3	43.8	50.0	0.0	62.5	50.0	50.0	0.0	25.0
	P	0.436	0.914	NA	0.697	0.526	0.751	NA	0.327
Insurance	CBHI	24.2	46.9	48.4	50.8	25.0	34.4	32.3	67.2
	Other insurance	43.8	50.0	0.0	62.5	50.0	50.0	0.0	25.0
	P	0.436	0.914	NA	0.697	0.526	0.751	NA	0.327
Type of hemophilia	A	27.3	38.5	48.4	44.5	18.8	28.1	32.3	48.4
	B	25.0	58.3	45.8	58.3	33.3	37.5	36.1	70.8
	P	0.884	0.227	0.930	0.500	0.536	0.747	0.864	0.428
Severity	Moderate	35.0	45.0	42.5	37.5	40.0	45.0	30.0	47.5
	Severe	15.6	50.0	43.8	70.3	12.5	25.0	27.1	81.3
	P	0.204	0.784	0.967	**0.048**	0.254	0.516	0.897	0.204
Bleeding episodes	None	39.1	45.8	81.3	40.6	31.3	46.9	52.1	37.5
	≥ once per month	43.8	50.0	0.0	62.5	50.0	50.0	0.0	25.0
	P	0.498	0.977	NA	0.466	0.925	0.602	NA	0.655

Student t-test

CHAPTER FIVE: DISCUSSION

DEMOGRAPHIC AND CLINICAL CHARACTERISTICS

In our study, we found that more than half of the children have severe hemophilia (52%), while almost all (96.3%) were on demand as treatment option. A large percentage (47%) of children receive plasma derivatives (FFP or cryoprecipitate) when they bleed, which shows similar management problems with the unavailability of factor concentrates in Rwanda as in other developing countries, as pointed out by Ghosh et al (19).

In our study we found that many children miss school due to serious illness, they also have difficulty traveling for a long distance to the hemophilia center explained by a large number of children who come to the province, they have a lot of trouble getting the transfer to consult at CHUK as many of them used CBHI (mituelle de sante), means of transport: as many mothers had a low socio-economic status and a low level of education which explained less work for caregivers, all explaining several barriers to hemophilia care as studied by K Saxena et al(31).

QUALITY OF LIFE OF HEMOPHILIAC CHILDREN AND THEIR PARENTS

The QOL study as an important method to assess the medical care received by hemophiliac patients was carried out using long version Haemo-QoL questionnaires.

The questionnaire explored many dimensions that involve almost all aspects of the well-being of children and their parents, helping to discuss the overall QOL of the pediatric hemophilia population and the areas most affected. The overall QOL in our study was poor in children with hemophilia and their parents, reflecting similar results with other studies in Indian, Iranian, Iraqi, Turks and Egyptian children(8,22–25). The QoL assessment of Filipino children was a little better(26). To be interpreted with caution since majority of the respondents had moderate disease in Filipino as compared with our Rwandan, Turks and Egyptian children where majority of them had severe hemophilia.

A Colombian study found HR-QoL in PWH same as in the general population, but almost of PWH were on prophylaxis(17).

This study showed a subscale of feelings like the aspects of life that had the greatest impact on the poor QOL of children aged 8 to 12, like their parents, which explains a state of mind and worse emotional consequences for hemophilia. Teenagers were more concerned about their future, as this study shows. Children in these age groups are able to see the cause and effect of situations for themselves, this elaborate deterioration in the psychological aspect of life in this population explaining how hemophiliac children are stressed, sad and sometimes depressed. This highlights the need for psychological support in our center, because psychoeducational interventions in other studies were deemed useful to promote a feeling of self-efficacy and better self-management skills when targeting young people (children and adolescents) with hemophilia(32).

The treatment subscale was affected in the parent group I report, which shows how young children ≤ 7 years old perceive care and the side effect on the disease, this can be explained by many factors, including understood the challenges faced by parents when their children bleed: long travel to the hematology clinic as a single treatment center across the country, sometimes lack of factor concentrate at the treatment center, no prophylaxis protocol available in the country and frequent bleeding requiring several injections.

Family subscale was impaired in parents' group III respondents which explains how older children are overprotected and their parents prevent them from interacting with their peers, similar observation observed while comparing HRQoL as reports of children versus reports of parents of HRQoL with parents of older children who are more concerned than their children about participating in sports and school activities. This indicates great bleeding concern in parents of elder children with severe disease, which demonstrates the chronic problem that there is no prophylaxis protocol available in our center; unlike the study by Bagheri et al in Shiraz, Iran, where supervision and parental control were more important in young children than in adolescents (23).

A review by Giordano and colleagues noted that children living with hemophilia need to socialize and live in community, can and should perform physical activities safely, and must be informed of their condition in order to manage their normal adult life(33).

In our study, the injection subscale obtained a low score (20%) in all areas, the drug is administered by a nurse from our center, because almost all children must go to nearest health facility for injections, which is considered to have a positive impact on the QOL of our population.

CORRELATION BETWEEN HRQOL AND DEMOGRAPHIC CHARACTERISTICS VARIABLES

In group II of children who responded, school absenteeism was correlated with a poor QOL on feelings, family, other people and treatment subscales, demonstrating that mood and emotions alteration due to disease, restriction and limitation of physical activity in relation to peers at school and the unsatisfactory treatment option contribute to the low school attendance of children with hemophilia. Shapiro et al study found that children with hemophilia may not reach their full potential at school and later in life due to a higher frequency of bleeding episodes(6).

Adolescents with severe hemophilia were affected by the way they maintain relationships and activities with their friends compared to those with moderate illness, and those who have one or more bleeds were more affected by how they consider their future in relation to those who have not done so. The severity of hemophilia relates with the frequency of bleeding and the way it affects QOL is consistent with other studies, including the study by D Espaldon and colleagues which showed how severe disease affects the way children see themselves, how they participate in school activities, and how they see their future(26). A study by Tantawy et al in Egyptian children with hemophilia has shown impaired physical health subscale, which means reduced mobility, pain and inability to perform basic activities in children with severe illness (22).

In the report of parents in group I, young children $\leq$ 7 years old in rural areas (provinces) have a strong deterioration in the field of physical health compared to those in the city of Kigali, which explains the challenges that face on this subscale linked to the distance from the hematology center. In group II of responding parents, parents of children aged 8 to 12 using CBHI insurance were more concerned with how their children interacted with others and the treatment they received compared to parents using other type of insurance, explaining personal expenses and referral problems among those who use CBHI insurance. This study finding is similar to the study by K. Saxena et al, which highlighted various barriers to hemophilia care, including distance from hemophilia center and barriers issues related to the cost of factor concentrates and insurance cost limit as factors that reduce QOL (31).

In this research, also parents of young children with severe hemophilia had altered family dimensions compared to those with moderate disease explaining parental overprotection in young children with severe disease as in other studies in Iran and India(23,24).

CHALLENGES AND LIMITATION

The limitation of the study was the small population studied for the generalization of research, the similar limited publication in the region and taking into account only the report from parents on the evaluation of the QOL of young children without complete reliable information on the their QOL.

CHAPTER SIX: CONCLUSION AND RECOMMENDATIONS

CONCLUSION

This study aimed to evaluate the QOL of children living with hemophilia and their parents in Rwanda by using the Hemo-Qol questionnaire and identify the important factors that contribute to QOL. QOL was poor in Rwandan hemophiliac population. The feeling and future subscales in children and the treatment, feeling and family subscales in parents mainly contributed to the poor QOL in our study. The injection subscale explained in our study that the administration of drugs by a nurse seems to have had a positive impact on QOL.

The studied clinical and demographic data indicated that many of our children were suffering from a serious illness and almost all treatments on demand. This study also showed that children who miss school have a reduced Qol in addition to those with severe hemophilia, frequent bleeding episodes, long distance to the hemophilia treatment center and those whose parents use public insurance(CBHI) as factors contributing to children poor QOL.

RECOMMENDATIONS

The health system and its stakeholders must improve hemophilia management strategies, focusing on medical care, promotion of the use of prophylaxis and psychosocial education for parents and children with hemophilia. Hemophilia care should be seen as other chronic diseases across the Rwandan Ministry of Health through the idea of education to support human resources, assist a well-established and well-equipped hemophilia treatment center(HTC) in the country and advocacy for prophylaxis. Pediatricians and other health care providers at CHUK should establish psychological education policies as primary strategies to ameliorate the QOL in hemophilia care.

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ANNEXES

QUESTIONNAIRE

SECTION I: DEMOGRAPHIC AND CLINICAL CHARACTERISTICS QUESTIONNAIRES		
NO	**QUESTION**	**ANSWER**
1.	Date	
2.	Initials of the parent's name	
3.	Age of parent (In years)	18-45 45-55 >55
4.	Sex	Male Female
5.	Place of origin	Kigali City Northern Province Southern Province Eastern Province Western Province
6.	Religion	Christian Muslim Others
7.	Relationship with the patient(if guardian or parents)	Mother Father Sister/Brother Other
8.	Social categories/Ubudehe	Category 1 Category 2 Category 3

		Category 4
9.	Medical insurance	MUTUELLE RSSB CORAR MEDIPLAN RADIANT UAP MMI PRIVATE OTHERS NONE
10.	Occupation of the caretaker	Employed Self-employed Unemployed
11.	Level of education of the caretaker	Illiterate Primary school High school University
12.	Type of hemophilia	Hemophilia A Hemophilia B
13.	Severity of hemophilia	Mild

		Moderate Severe
14.	Type of treatment	On- demand Prophylactic
15.	Type of product received when bleeding occurred	Plasma-derived product (FFP or CRYOPRECIPITATE) Recombinant factor VIII or IX
16.	number of bleeding in the 4 weeks	None 1 -5 bleeding/month >5 bleeding/month
17.	Site of bleeding	Joint Other site
19.	number of school absences in the last 4 weeks	None Once/month More than once/month

CMHS/IRB ETHIC COMMITTEE APPROVAL

UNIVERSITY of RWANDA

COLLEGE OF MEDICINE AND HEALTH SCIENCES

DIRECTORATE OF RESEARCH & INNOVATION

CMHS INSTITUTIONAL REVIEW BOARD (IRB)

Kigali, 15th /October/2019

Dr NTIYAMIRA Jean Claude
School of Medicine and Pharmacy, CMHS, UR

Approval Notice: No 483/CMHS IRB/2019

Your Project Title ***"Assessment of Health-Related Quality Of Life in Rwandan Children with Hemophilia"*** has been evaluated by CMHS Institutional Review Board.

Name of Members	Institute	Involved in the decision		
		Yes	No (Reason)	
			Absent	Withdrawn from the proceeding
Prof Kato J. Njunwa	UR-CMHS	X		
Prof Jean Bosco Gahutu	UR-CMHS	X		
Dr Brenda Asiimwe-Kateera	UR-CMHS	X		
Prof Ntaganira Joseph	UR-CMHS			X
Dr Tumusiime K. David	UR-CMHS	X		
Dr Kayonga N. Egide	UR-CMHS	X		
Mr Kanyoni Maurice	UR-CMHS		X	
Prof Munyanshongore Cyprien	UR-CMHS	X		
Mrs Ruzindana Landrine	Kicukiro district		X	
Dr Gishoma Darius	UR-CMHS	X		
Dr Donatilla Mukamana	UR-CMHS	X		
Prof Kyamanywa Patrick	UR-CMHS		X	
Prof Condo Umutesi Jeannine	UR-CMHS		X	
Dr Nyirazinyoye Laetitia	UR-CMHS	X		
Dr Nkeramihigo Emmanuel	UR-CMHS		X	
Sr Maliboli Marie Josee	CHUK	X		
Dr Mudenge Charles	Centre Psycho-Social	X		

After reviewing your protocol during the IRB meeting of where quorum was met and revisions made on the advice of the CMHS IRB submitted on 14th October 2019, **Approval has been granted to your study.**
Please note that approval of the protocol and consent form is valid for **12 months**.

You are responsible for fulfilling the following requirements:

1. Changes, amendments, and addenda to the protocol or consent form must be submitted to the committee for review and approval, prior to activation of the changes.
2. Only approved consent forms are to be used in the enrolment of participants.
3. All consent forms signed by subjects should be retained on file. The IRB may conduct audits of all study records, and consent documentation may be part of such audits.
4. A continuing review application must be submitted to the IRB in a timely fashion and before expiry of this approval
5. Failure to submit a continuing review application will result in termination of the study
6. Notify the IRB committee once the study is finished

Sincerely,

Date of Approval: The 15th October 2019

Expiration date: The 15th October 2020

Professor GAHUTU Jean Bosco
Chairperson Institutional Review Board,
College of Medicine and Health Sciences, UR

Cc:
- Principal College of Medicine and Health Sciences, UR
- University Director of Research and Postgraduate Studies, UR

CHUK ETHIC COMMITTEE APPROVAL

Review Approval Notice

Dear Jean claude NTIYAMIRA,

Your research project: ***"ASSESSMENT OF HEALTH-RELATED QUALITY OF LIFE IN RWANDAN CHILDREN WITH HEMOPHILIA "***

During the meeting of the Ethics Committee of University Teaching Hospital of Kigali (CHUK) that was held on 13,Dec,2019 to evaluate your request for ethical approval of the above mentioned research project, we are pleased to inform you that the Ethics Committee/CHUK has approved your research project.

You are required to present the results of your study to CHUK Ethics Committee before publication by using this link:www.chuk.rw/research/fullreport/?appid=15&&chuk.

PS: Please note that the present approval is valid for 12 months.

Yours sincerely,

Dr Emmanuel Rusingiza Kamanzi
The Chairperson, Ethics Committee,
University Teaching Hospital of Kigali