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# THE EFFECT OF HEMOPHILIA ON HEALTH RELATED QUALITY OF LIFE IN EGYPTIAN CHILDREN

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**Abstract**

**Background:** Hemophilia can have a huge negative impact not only on the physical health but also on the psychological, economic and social well-being of the affected children and their family. This study aimed to study the effect of Hemophilia on Health related Quality of Life in Egyptian Children using an Arabic version of (EQ-5D-5L and EuroQoL Egypt) questionnaire. **Methods:** This study was carried out during outpatient visits in the Department of Pediatrics Hematology and Oncology Unit at Zagazig University Children Hospital on 48 cases ranged from 4-16 years during the period from January 2021 to August 2021 on 48 patients, patients were divided equally into 2groups group I included 24 children from (4 to 10 years) had had hemophilia A and Group II 24 children from (11 to16 years) had had hemophilia B. **Results:** In our study , It was found that most frequent manifestation in younger patients were hemarthrosis (70.8%) followed by epistaxis (62.5%) and bleeding after circumcision (60.4%) , while in older patients , most frequent manifestation were hemarthrosis (87.5%) followed by bleeding after circumcision (75%) that reflect bad quality of life in older age group (10-16 years) which was attributed to frequent bleeding events and its complication. Conclusions: Subscale impairments, severity of hemophilia, barriers to hemophilia care, presence of support groups are factors that significantly affect and predict the QOL of Egyptian children with hemophilia. Addressing these concerns may amplify their understanding of the disease and further improve their quality of life.

**Keywords:** Chronic pain, Hemophilia, Pain management, Prophylaxis

## Introduction

Hemophilia is a rare, chronic, the hereditary bleeding disorder caused by a defective factor VIII or factor IX (plasma clotting factor), leading to impaired clotting characterized by spontaneous bleeding and excessive bleeding after surgery or trauma. There are two most common forms of hemophilia, hemophilia A and hemophilia B. Children with severe hemophilia have frequent, spontaneous bleeding episodes that usually involve major joints, muscles, or soft tissues and may lead to residual morbidity. These morbidity indicates that hemophilic children had a diminished quality of life. [(1)]

The assessment of health-related quality of life (HRQoL) in haemophilia as a patient-reported outcome provides direct information about haemophilia patients' general well-being as well as the effects of haemophilia and treatment outcomes. The generic assessment of HRQoL in haemophilia started in 1990. Subsequently, both generic and disease-specific instruments have been used to assess the HRQoL of haemophilia patients. The EQ-5D Questionnaire IS generic HRQoL instruments [(2)].

The quality of life related to the health (QOLRH) may be influenced by factors such as the disease and its treatment, the manner in which the person copes with his/her problem and the access to care. In the case of hemophilia, the factors which stand out are: restrictions to physical activities, the concern about hemorrhages that may be life-threatening, the development of arthropathy, the need for orthopedic procedures and infectious diseases, vectorized by blood or hemoderivatives [(3)].

This study aimed to study the effect of Hemophilia on Health related Quality of Life in Egyptian Children using an Arabic version of (EQ-5D-5L and EuroQoL Egypt) questionnaire

## Methods

This study was carried out during outpatient visits in the Department of Pediatrics Hematology and Oncology Unit at Zagazig University Children Hospital on 48 cases ranged from 4-16 years during the period from January 2021 to August 2021 on 48 patients, patients were divided equally into 2groups group I included 24 children from (4 to 10 years) had had hemophilia A and Group II included 24 children from (11 to16 years) had hemophilia B

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Written informed consent was obtained from all children's' parents or their relatives and the study was approved by the research ethical committee of Faculty of Medicine, Zagazig University (International review board IRB#:6752-30-1-2021). The study was done according to The Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans.

**Inclusion criteria:**

- ✓ Age is 4-12 years.
- ✓ Has no co-morbidconditions.

**Exclusion criteria:**

- ✓ Children with cognitive impairment resulting from central nervoussystem
- ✓ Children with any psychiatric disorder e.g autism

**All participants were subjected to**

Full history taking and physical examination: Including the frequency of bleeding attacks, sites, severity, and the frequency of administration of factor VIII preparations and the types used. The presence of hemarthrosis, muscle hematoma, target joint, and limitation of the movement of any affected joint was particularly assessed during examination , history of bleeding during circumcision, epistaxis , gum bleeding, bleeding after dental procedures, any previous surgery, and were asked for a history of intracranial hemorrhage.

**The social class:**

The social class was calculated using Sherbiny method for social class calculation. The participant were asked about occupation, education,income index .

Occupation was scored as follow :1 =worker , 2 =skilled , 3=employee , 4= specialist

Education was scored as follow :1= Illiterate , 2= Educated

Income was scored as follow :1=Not enough , 2= Enough , 3= Enough and exceed

The total score was calculated and the cases was divided as lowsocial class less than or equal 50% and high social class more than 50%.

HRQoL was measured using The EQ-5D-5L is a Health-Related Quality of Life (HRQoL) instrument for describing and valuing health of PWH. It is a Patient-Reported Outcome (PRO) tool used in clinics and studies across the world. It based on a descriptive system that defines health in terms of 5 dimensions, rated on a scale of 1-5:

1. Mobility
2. Self-care
3. Usual Activities
4. Pain / discomfort
5. Anxiety / Depression

**Statistical analysis**

All data were collected, tabulated and statistically analyzed using SPSS 22.0 for windows (SPSS Inc., Chicago, IL, USA) and MedCalc 13 for windows (MedCalc Software bvba, Ostend, Belgium). Continuous variables were expressed as the mean ± SD and the categorical variables were expressed as a number(percentage). Continuous variables were checked for normality by using Shapiro-Wilk test. Mann Whitney U test was used to compare between two groups of non-normally distributed variables. Wilcoxon signed ranks test was used to compare between two dependent groups of non-normally distributed variables. All tests were two sided. p-value $< 0.05$ was considered statistically significant (S), p- value $< 0.001$ was considered highly statistically significant (HS), and p- value $\geq 0.05$ was considered statistically insignificant (NS).

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## Results

**Table (1): Demographic and socioeconomic characteristics of parents ofboth age groups**

| Characteristics | Group I (N=24) | | Group II (N=24) | |
|---|---|---|---|---|
| | No. | % | No. | % |
| | | | | |
| **Educational level of parents** | | | | |
| Illiterate | 5 | 20.8% | 6 | 25% |
| Educated | 19 | 79.2% | 18 | 75% |
| **Occupation of father** | | | | |
| Worker | 7 | 29.1% | 8 | 33.3% |
| Skilled | 12 | 50 % | 10 | 41.7% |
| Employee | 5 | 20.9% | 6 | 25 % |
| Specialist | - | | - | |
| **Income** | | | | |
| Not enough | 4 | 16.6% | 5 | 20.9% |
| Enough | 15 | 62.5% | 33 | 66.6% |
| Enough and exceed | 5 | 20.9% | 3 | 12.5% |
| **Socio-economic status** | | | | |
| Low | 19 | 79.1% | 39 | 81.3% |
| High | 5 | 20.9% | 9 | 18.8% |

This table shows demographic and socioeconomic characteristics ofparents of both age groups. about 79.2 % educated ; 29.1 % worker ; 50 % Skilled ; 20.9% Employee, about 62.5 % have enough income ; 16.6% not enough ; 20.9% Enough and exceed . about 79.1%low Socio- economic status ;20.9 7%high Socio-economic status .

**Table (2): Medical characteristics and clinical data of both age groups**

| Characteristics | Group I (N=24) | | Group II (N=24) | | $\chi 2$ | P |
|---|---|---|---|---|---|---|
| | No. | % | No. | % | | |
| **Severity of disease** | | | | | | |
| Moderate | 9 | 37.5% | 8 | 33.3% | 0.19 | 0.67 |
| Severe | 15 | 62.5% | 16 | 66.7% | | NS |
| **Clinical picture** | | | | | | |
| Circumcision bleeding | 15 | 62.5% | 18 | 75% | 2.33 | 0.13 NS |
| Epistaxis | 15 | 62.5% | 13 | 54.1% | 1.06 | 0.30 NS |
| Gum bleeding | 13 | 54.1% | 14 | 58.3% | 0.38 | 0.54 NS |

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| | | | | | | |
|---|---|---|---|---|---|---|
| Bleeding after dental procedure | 6 | 25% | 11 | 45.8% | 4.55 | 0.03* S |
| Previous surgery | 5 | 20.8% | 8 | 33.3% | 2.56 | 0.10 NS |
| Intracranial hemorrhage | 2 | 8.3% | 0 | 0% | 3.10 | 0.08 NS |
| Hemarthrosis | 17 | 70.8% | 21 | 87.5% | 4.04 | 0.04* S |
| Muscle hematoma | 12 | 50% | 13 | 54.2% | 0.17 | 0.68 NS |
| Target joint | 15 | 62.5% | 16 | 66.7% | 0.42 | 0.52 NS |
| Limited joint movement | 16 | 66.7% | 20 | 83.3% | 4.38 | 0.04* S |

NS non significant ;S significant .

This table shows that there was statistical significance difference between the two studied groups in frequency of bleeding after dental care, hemarthrosis and limited joint movement with increase all among Group II. No differences was found in other clinical findings or other medical characteristics .

**Table (2430): Comparison HRQoL dimensions between two age groups according to (children report):**

| HRQoL (child report ) | Group I (N=24) | Group II (N=24) | t | P |
|---|---|---|---|---|
| Physical health | 70.05± 15.84 | 76.01 ± 13.45 | 1.99 | 0.06 NS |
| View(attitude) | 53.02 ± 17.09 | 63.32 ± 11.53 | 3.46 | <0.001** |
| Family | 68.43 ± 11.11 | 78.38 ± 9.89 | 4.63 | <0.001** |
| Friends | 55.20 ± 17.02 | 68.75 ± 20.48 | 3.52 | <0.001** |
| Sports & school | 62.18 ± 13.01 | 76.76 ± 12.19 | 5.76 | <0.001** |
| Dealing(Coping) | NI | 39.02 ± 9.48 | | |
| Treatment | 67.05 ± 8.82 | 68.95 ± 12.58 | 0.68 | 0.39 NS |
| Total score | 61.36 ± 7.89 | 67.92 ± 10.39 | 3.48 | 0.001** |

This table shows that there was statistical highly significant difference between the two studied groups in view, family, friends, sport and school and total score with increase all among Group II.

**Table (4): Comparison HRQoL dimensions between two age groups according to (Parents report):**

| HRQoL (Parents report) | Group I (N=24) | Group II (N=24) | t | P |
|---|---|---|---|---|
| Physical health | 72.39 ± 13.75 | 77.57 ± 10.33 | 2.09 | 0.04* |
| View(attitude) | 52.40 ± 12.67 | 69.69 ± 10.34 | 7.32 | <0.001** |
| Family | 67.39 ± 9.33 | 77.21 ± 8.69 | 5.33 | <0.001** |
| Friends | 64.58 ± 13.48 | 57.94 ± 14.74 | 2.30 | 0.02* |
| Sports & school | 71.45 ± 10.16 | 76.75 ± 11.53 | 2.38 | 0.02* |

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| | | | | |
|---|---|---|---|---|
| Dealing(coping) | NI | 42.59 ± 8.18 | | |
| Treatment | 68.86 ± 8.39 | 74.21 ± 10.12 | 2.82 | 0.006** |
| Total score | 63.46 ± 6.59 | 69.85 ± 8.63 | 4.08 | <0.001** |

This table shows that there was statistical significance difference between the two studied groups in physical health, view, family, friends, sport and school, treatment and total score with increase all among Group II .

**Table (5): Effect of severity of Hemophilia on HRQoL (children and parents report) among group I (4-10 years).**

| **Children** | Group I (4-10 years) N=24 | | Test• | p-value (Sig.) |
|---|---|---|---|---|
| | Moderate hemophilia (N=8) Mean ± SD | Severe hemophilia (N=16) Mean ± SD | | |
| Physical health | 58.08 ± 15.89 | 76.61 ± 11.52 | -3.843 | <0.001 (HS) |
| View (attitude) | 52.94 ± 21.43 | 68.54 ± 11.12 | -2.690 | 0.007 (S) |
| Family | 74.26 ± 12.07 | 80.64 ± 7.79 | -1.826 | 0.068 (NS) |
| Friends | 50.00 ± 0.00 | 63.54 ± 24.29 | -2.078 | 0.038 (S) |
| Sports & school | 64.66 ± 14.28 | 76.30 ± 10.34 | -2.924 | 0.003 (S) |
| Treatment | 73.52 ± 6.06 | 74.19 ± 15.11 | -0.412 | 0.680 (NS) |
| Total score | 59.62 ± 11.15 | 72.47 ± 6.52 | -3.950 | <0.001 (HS) |
| **Parents** | | | | |
| Physical health | 60.66 ± 14.61 | 78.83 ± 7.85 | -4.397 | <0.001 (HS) |
| View (attitude) | 55.35 ± 17.90 | 70.12 ± 10.04 | -2.890 | 0.004 (S) |
| Family | 73.52 ± 9.51 | 79.23 ± 7.63 | -2.022 | 0.043 (S) |
| Friends | 51.47 ± 10.71 | 71.77 ± 8.51 | -5.069 | <0.001 (HS) |
| Sports & school | 67.11 ± 14.87 | 77.38 ± 7.20 | -2.515 | 0.012 (S) |
| Treatment | 72.79 ± 10.11 | 75.00 ± 10.20 | -0.708 | 0.479 (NS) |
| Total score | 62.43 ± 9.71 | 73.92 ± 4.24 | -4.106 | <0.001 (HS) |

Mann Whitney U test. p-value< 0.05 is significant. Sig.: significance

This table shows that there was statistical significance difference between moderate and severe cases in Group I children report in feeling, view, friends, other people, sport & school and total score with increases all among severe cases. Regarding parents report that there was statistical significance difference between moderate and severe cases in all items except treatment with increases all among severe cases.

**Table (6): Effect of severity of Hemophilia on HRQoL (children & parents report) among group II (11-16 years).**

| | Group II (11-16 years) N=24 | Test• | p-value (Sig.) |
|---|---|---|---|

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| Children | Moderate hemophilia(N=8) Mean ± SD | Severe hemophilia (N=16) Mean ± SD | | |
|---|---|---|---|---|
| Physical health | 60.21 ± 11.98 | 83.19 ± 5.74 | -5.240 | <0.001 (HS) |
| Feeling | 45.18 ± 11.42 | 65.47 ± 7.34 | -5.133 | <0.001 (HS) |
| View (attitude) | 53.68 ± 12.91 | 67.70 ± 7.67 | -3.670 | <0.001 (HS) |
| Family | 65.00 ± 11.95 | 70.00 ± 10.53 | -1.173 | 0.241 (NS) |
| Friends | 45.00 ± 11.13 | 59.84 ± 10.13 | -3.077 | 0.002 (S) |
| Other people | 45.52 ± 10.96 | 54.63 ± 10.13 | -2.308 | 0.021 (S) |
| Sports & school | 62.28 ± 14.77 | 77.53 ± 6.91 | -3.736 | <0.001 (HS) |
| Treatment | 63.30 ± 9.49 | 70.20 ± 7.71 | -2.360 | 0.018 (S) |
| Total score | 53.68 ± 7.20 | 64.85 ± 5.34 | -4.530 | <0.001 (HS) |
| **Parents** | | | | |
| Physical health | 66.62 ± 8.83 | 82.55 ± 6.41 | -4.713 | <0.001 (HS) |
| Feeling | 59.39 ± 10.16 | 74.37 ± 6.28 | -4.624 | <0.001 (HS) |
| View (attitude) | 53.54 ± 8.75 | 68.57 ± 9.84 | -3.928 | <0.001 (HS) |
| Family | 66.66 ± 11.12 | 67.72 ± 8.57 | -0.216 | 0.829 (NS) |
| Friends | 49.58 ± 11.44 | 61.74 ± 14.63 | -2.940 | 0.003 (S) |
| Other people | 52.74 ± 10.16 | 55.28 ± 9.67 | -0.170 | 0.865 (NS) |
| Sports & school | 63.52 ± 9.92 | 75.06 ± 8.10 | -3.492 | <0.001 (HS) |
| Treatment | 63.32 ± 10.74 | 71.39 ± 5.65 | -2.328 | 0.020 (S) |
| Total score | 57.22 ± 6.53 | 66.29 ± 4.32 | -4.518 | <0.001 (HS) |

**Mann Whitney U test. p-value< 0.05 is significant. Sig.: significance**.

This table shows that there was statistical significance difference between moderate and severe cases in Group II children report in all items except family and support with increases all among severe cases. Regarding parents report that there was statistical significance difference between moderate and severe cases in all items except family, support, other people and dealing with increases all among severe cases.

## Discussion

Hemophilia A is an X chromosome–linked recessive hemorrhagic disorder that is characterized by impaired factor VIII (FVIII) production. The worldwide incidence of hemophilia A is approximately 1 case per 5000 male individuals, with approximately one third of affected individuals not having a family history. Quality of life (QoL) of childrenwith chronic conditions, such as hemophilia, has received increasing attention in recent years. It can be defined—in analogy to the World Health Organization(WHO)definition of health—as patient-perceived well-being and function in terms of physical, emotional, mental, social, and behavioral life domains [(4)].

The aim of this study was to improve the current status of health related quality of life (HR-QOL) in pediatric population with hemophilia using an Arabic version of (EQ-5D-5L and EuroQoL Egypt) questionnaire

In our study, It was found that most frequent manifestation in younger patients were hemarthrosis followed by epistaxis and bleeding after circumcision, while in older patients , most frequent manifestation were hemarthrosis followed by bleeding after circumcision .that reflect bad quality of life in older age group(10-16 years) which was attributed to frequent bleeding events and its complication. about 79% of the patients suffered from hemarthrosis, 87.5% for agegroup II, while 70.8% for age group I which statistically significant that reflect bad quality of life in older age group.

**Goto et al [(5)]** Hemophilic arthropathy (HA) causes major morbidity in patients with hemophilia (PWH) with most commonly affected joints being knees, ankles, and elbows. Thus, repeated intra-articular bleeding

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affects the progression of HA. In addition, pain caused by the intra-articular bleeding and HA significantly impacts activities of daily living and quality of life in PWH

It was found that about 67.7% of our the patients have bleeding after circumcision,high in group II (75 %)while (60.4 %) in group I .also Tantawy et al .2011 reported that episode of first bleeding was high among older age group .possibly reflecting improved awareness for screening children for bleeding tendency prior to circumcision in the recent years.

Regarding target joint affection we found that there were about(65.6%) of our patients have target joint: (62.5%) of them among age group I and (68.8%) among age group II, While **Bullinger et al.** [6] reported that 50.3% of the children have a target joint: 61% of the oldest children in comparison to 38.9% in age group I.

In our study, 73.9% of the patients reported to have limitation of the joint movement, it was statistically significant in older age (group II) compared to age group I. Also, **Tantawy et al** [4] reported 63.5% of the patients have limitation of the joint movement, it was statistically highly significant in older age group compared to other age groups (P = 0.005).

In this study it was found that older patients could predict the bleeding episodes before it occurred more frequently than younger patients by a strange feeling that they noticed before bleeding as 52.1%of older patients always predict the bleeding episode and 4.2% never , while in younger age only 31.3% sometimes could predict the bleeding episodes, **St-Louis et al** [7] reported that statistically it was reported to be 66.7% of the patients could predict the strange feeling before bleeding .

Regarding to HRQoL dimensions in comparison between the two studied groups as regard children report our study showed that there was statistically significant better quality of life in younger age group (4-7 years ) than older one ( 8-12years ) in view, family, friends, sport and school and total score .

Younger children (group I) , showed most impairment in the scale of Physical health also in Family scale ,which was attributed to parental supervision, with parents exerting more control over their children, thus keeping the patient away from interacting with friends and participatingin physical activities. **Espladon and Hernandez,** [8] report that GroupI child respondents showed also most impairment in the scale of Family which was attributed to parental supervision .

While older children (Group II) were most impaired in the scale of Family as younger group in addition to Sports & School scale. Like the younger children, over protectiveness may be the reason, this time from the teachers and school administrators that may prevent them from participating in school activities. Parents, particularly mothers, and caregivers tend to overprotect because they perceive their child to be more susceptible and at risk because of his illness. **Grayson et al.,** [9] in their study of 68 families with a chronically ill child, have illustrated that over protectiveness has detrimental effects on the growing child such as symptoms of depression and oppositional behavior. Over protective parents are also less expected to grant independence to their child in the future. Parents may be torn between allowing self-sufficiency to their child and the need to protect the child from injuries and further medical harm.

Group II also show high impairment in physical health (76.01 ± 13.45) Which reflect more bleeding events and affection of their joints.

According to parents report, there was statistical significance difference between the two studied groups in physical health, view, family, friends, sport and school, treatment and total score with increase all among Group II ,which reflect better quality of life in groupI, Parents‘ scores reflect similar areas of most impairment as the child‘s in Group I parents had most impairments in the scale of Physical health alsoin the scale of Sport &school, while Groups II parents showed most impairments in the scale of physical health , family and sport &school , which agree with **Espladon and Hernandez** [8] who report Group II parents showed most impairments in the scale of Sports and School.

In comparison between child- parent responses , we found that childhad better quality of life than their parents in both age groups , in most scales indicating more stressful , emotional and bad quality of life in parent and better acceptance, less emotional concerns and better adaptation of child with his illness than his parent.Which agree with **Beeton et al. (10)** . who stated that parents are affected by how their child communicates the way they feel about their illness and how well these children adapt to their disorder.

**Conclusion**

Subscale impairments, severity of hemophilia, barriers to hemophilia care, presence of support groups are factors that significantly affect and predict the QOL of Egyptian children with hemophilia. Addressing these concerns may amplify their understanding of the disease and further improve their quality of life.

**Availability of data and materials**

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request

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**Conflicting Interest (If present, give more details):** No Conflict of Interest

**No financial disclosure**

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Not applicable

**Declarations**

**-Ethics approval and consent to participate**

Written informed consent was obtained from all patients and the study was approved by the research ethical committee of Faculty of Medicine, Zagazig University (International review board IRB#:6752-30-1-2021). The study was done according to The Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans.

**-Consent for publication**

Not applicable

**Competing interests**

The authors declare that they have no competing interests.

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