Original Article

Adults Hemophiliacs In Pakistan: Health Related Quality Of Life And Psychological Aspects

Eesha Yaqoob[1], Zonaira Mushahid[2], Muhammad Asad Asif[3], Muhammad Ishfaq[4], Maheen Sabah[5], Mishal Waseem[6]

[1] Ph.D. Sociology, PMAS Arid Agriculture.
[2] MBBS, DOW, University of Health Sciences.
[3] House Officer, RMU and Allied Hospitals, Rawalpindi.
[4] MPhil, Rural Sociology, University of Agriculture, Faisalabad.
[5] MBBS, MSPH, Health Services Academy, Islamabad.
[6] BS Psychology, Bahria University Islamabad.

Author's Contribution
[1] *Conception of study*
[1,4,5] *Experimentation/Study Conduction*
[1,2,3,5,6] *Analysis/Interpretation/Discussion*
[1,2,3,5,6] *Manuscript Writing*
[1] *Critical Review*
[1,2,3,4,6] *Facilitation and Material analysis*

Corresponding Author
Dr. Eesha Yaqoob
Ph.D. Sociology
PMAS Arid Agriculture
Rawalpindi
Email: innocenteesha@yahoo.com

Article Processing
Received: 11/10/2022
Accepted: 01/01/2023

Cite this Article: *Yaqoob, E., Mushahid, Z., Asif, M. A., Ishfaq, M. ., Sabah, M., & Waseem, M. (2023). Adult Hemophiliacs in Pakistan: Health-Related Quality of Life and Psychological Aspects. Journal of Rawalpindi Medical College, 27(1).*
DOI: https://doi.org/10.37939/jrmc.v27i1.2043

Conflict of Interest: *Nil*
Funding Source: *Nil*

Abstract

Objective: The goal of this investigation is to assess how psychological factors and pain affect adult hemophiliac patients' well-being.

Materials and Methods: On 102 hemophiliacs, a cross-sectional study was done. Data were gathered using visual analog scales for pain, depression anxiety stress assessments, and quality of life questionnaires specific to hemophilia. Regression analysis, analysis of covariance, and correlation coefficients were used to analyze the data. **Results:** According to the findings, 70.8% of hemophiliac patients felt pain on the research day. Patients with hemophilia had an average HRQoL score of 50.08 (standard deviation: 18.49). Additionally, stress, worry, and mild to serious depression were present in 45.7 %, 63.5%, and 58.3% of the patients, respectively. Additionally, a substantial correlation between HRQoL and sadness, anxiety, and pain intensity was found. The study variables were able to explain 47% of changes in HRQOL in the regression model, with depression and pain intensity serving as important predictors. Conclusion: To enhance the psychosocial health and quality of life of patients, emphasis should be given to these factors.

Key Words: Hemophilia, psychological factors, Pain

Introduction

A deficiency in coagulation factors VIII (FVIII) (in hemophilia A) or IX (FIX) (in hemophilia B) related to the X chromosome is the cause of hemophilia. [1] Recurrent musculoskeletal bleeding results in significant damage to the bones and cartilage, arthropathy, disability, and a decrease in quality of life due to bleeding in the joints, muscles, brain, and other internal organs. [2-5]

The disease has an impact on patients with hemophilia, but personality traits like coping and demographic factors like living situations can also have an impact on well-being. [6] According to studies, hemophiliacs had lower HRQoL than people in the general population.[7–9] The most frequent causes of impairment in the physical domain of HRQoL are joint pain and physical limitations. [10] Additionally, the physical (physical function, physical roles, and pain) and mental (social function, psychological health, and mental health) domains are linked to the lowest and highest HRQoL scores of hemophilia patients, respectively. [11]

The two main issues that patients with hemophilia worry about are the high cost of care and their poor perceptions of their bodies due to Arthropathy.[12] Chronic stress and depression are both present in some patients. [13] Different levels of depression and mood are experienced by hemophilia patients due to their pain and limitations[14]. The incidence of depression among elderly hemophiliacs in Italy was higher than that of the general population's age-matched group, and there was a link between depression and HRQoL.[15] Additionally, according to a study, pain and bleeding cause anxiety or depression in roughly half of young adults. [16] According to a different study, 43% of the patients had anxiety. Only about one-third of hemophiliacs said they did not experience anxiety or depression.[14]

Hemophilia patients may be affected by certain factors, such as depression brought on by low self-esteem in comparison to "normal" siblings and peers. Depression and the physical, psychological, and social dimensions of HRQoL have negative correlations, indicating a negative relationship between the two variables. [19]

Pain and HRQoL may be related in addition to psychological factors. [20] Patients with hemophilia live in pain due to recurrent bleeds in their muscles and joints. They experience "intense, unbelievable, terrible, annoying, and intolerable" [21] acute, ongoing, and constant pains that affect every aspect of their lives. [22]

Despite studies demonstrating reduced HRQoL in hemophilia patients, these studies were carried out in nations with greater access to healthcare than Pakistan, making them incomparable to our own. Plasma and clotting factors were extensively used in Iran since factor concentrates were hard to come by until a few years ago. [23] In Tabriz, Iran, there was only one study done on the well-being of young hemophiliac patients. [24] Children with this disease have been the subject of one study on anxiety and depressive symptoms. [25] A review of the literature also showed that there have only been a few studies on the relationship between patients with hemophilia's psychological characteristics and HRQoL.

The current study's objectives include determining the relationship between HRQoL, psychological variables, stress, depression, anxiety, and pain in adult hemophilia patients at a single treatment facility in Pakistan. It also aims to evaluate the quality of life (QoL), psychological variables, stress, depression, anxiety, and pain.

Materials and Methods

Study Design: Cross-sectional study design was used for the study.

Locale: The investigation was carried out in a hemophilia treatment center in Faisalabad.

Sample size: It was decided to select 102 participants.

Data Collection: Convenience sampling was employed to pick the participants. A total of 120 questionnaires were given out to patients, 111 of which were returned and 9 of which were insufficient. Of these, 102 were utilized for data analysis.

The Haem-A-QoL and the Depression Anxiety Stress Scale (DASS) were used in the study to collect data, along with a form for demographic and clinical information. The patientwas, educational level, marital status, type of hemophilia, disease severity, HIV and hepatitis status, bleeding history, site of bleeding, pain experience, pain severity (on a visual analog scale [VAS] ranging from 0 to 10), and occupation were all evaluated on the demographic and clinical characteristics form.

Table-1: Hemophilia patients' demographics and clinical characteristics

Variables	n (%)
Levels of Education	
Primary	14 (14.6)
Secondary	20 (18.7)
High school and diploma	28 (28.5)
Academic	40 (38.3)
Status of Marriage	
Single	52 (51.0)
Married	46 (45.0)
Divorced	4 (4.0)
Status of Occupation	
Self-employed	41 (65.9)
Employee	16 (22.3)
University student	7 (10.6)
Retired	2 (1.2)
Hemophilia's Type	
A	91 (88.3)
B	11 (11.7)
Disease' Severity	
Mild	25 (25.6)
Moderate	20 (21.6)
Severe	57 (52.8)
Type of Treatment	
FFP/Cryo	1 (0.1)
Factors concentrate	101 (99.9)
Status of Hepatitis	
Positive	38 (37.8)
Negative	64 (62.2)
HIV status	
Positive	1 (0.1)
Negative	101 (99.9)
Having pain	
Yes	72 (71.8)
No	30 (28.2)
Having bleeding	
Yes	86 (92.5)
No	16 (7.5)

ANALYSIS OF DATA

Version 21 of SPSS statistical software was used to examine the data. Validity and reliability (internal consistency, test-retest reliability) of the Haem-A-QoL were assessed psychometrically (convergent, known groups). Correlations between the Haem-A-QoL and DASS domains and pain intensity were assessed for convergence validity. The Spearmen and Pearson coefficient tests were used in accordance with the distribution. By contrasting patient subgroups with "no/mild" and "moderate/severe/extremely severe" symptoms, the validity of known groupings with regard to anxiety and depression was investigated. DescClinical, demographic, and psychological aspects were all included in descriptive statistics, which also included frequency, mean, and standard deviation (SD). The Kolmogorov-Smirnov test was initially used to determine whether the data was normal. The connection between pain intensity and HRQoL (r = 0.48, P.000), stress (r = 0.22, P.03), depression (r = 0.25, P.00), and anxiety (r = 0.31, P.003) was examined using an analysis of covariance (ANCOVA) model. Relationship between HRQoL and psychological factors, where pain severity was considered as a covariant. Patients with hemophilia were predicted using multiple regression analysis.

Results

Clinical and Demographic Characteristics

Data were analyzed for 102 eligible hemophilia patients with a mean age of 28.30 years (SD = 8.98). About 37.8% of participants had hepatitis, and slightly more than 52.8% had severe hemophilia. (Figure 1)

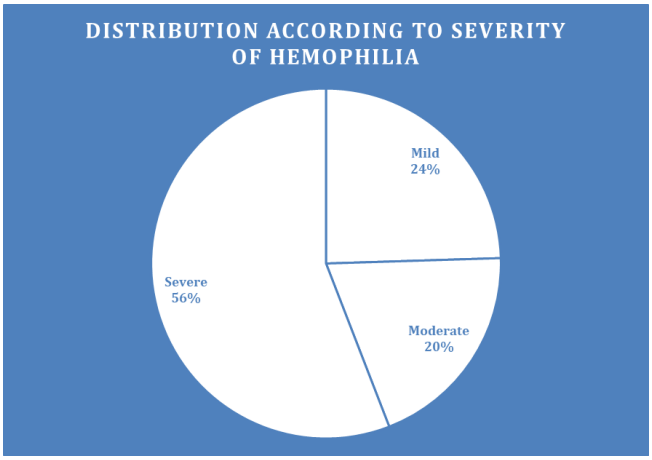

Figure-1 Distribution according to the severity of Hemophilia

Only one patient was found with HIV. In the previous six months, 92.5% of patients experienced bleeding (Table 1). (Figure 2)

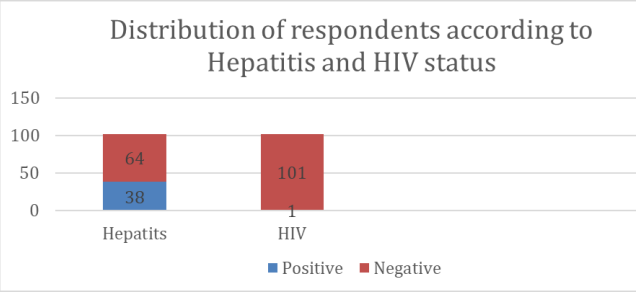

Figure-2: Distribution of respondents according to Hepatitis and HIV status

Thirteen individuals reported bleeding in muscle/soft tissue, with the majority of patients reporting bleeding in joints (n = 102) and mucosal membranes (n = 41). Of the 102 participants, 86 reported having bleeds within the past six months. Hematuria, epistaxis, and bleeding in the oral, urinary, gastrointestinal, and muscle systems were the most common types of bleeding. Factor concentrates were used to stop the bleeding in all of the patients. In fact, on the research day, 71.8% of the hemophiliac patients reported experiencing pain. The potential range for the maximum values in this cohort was 0.1 to 5.0, and the mean pain intensity score was 4.34 (SD = 1.62) (range 0-9).

Discussion

According to the results of the current study, about 71.8% of hemophiliac patients reported having pain on the VAS (potential range of 0-9), with a mean score of pain severity of 4.34 (SD = 1.62) in the group. In a European pain study using the verbal rating scale, the numeric rating scale, or the VAS (possible range 0 = no pain to 10 = pain as terrible as it could be), only 34% of hemophiliacs reported having pain levels this high.[26] According to self-reports on a 5-point scale, 33.3% of US young adult hemophilia patients reported having joint arthritic pain (possible range: 1 = no pain to 5 = severe pain all the time).[27] Additionally, According to the Wong-Baker Faces Pain Rating Scale (possible range of 0 = doesn't hurt at all to 10 = hurts as much as you can imagine), 20% of children and adolescents with bleeding disorders reported experiencing pain.

According to hemophilia treatment facilities in Faisalabad for Children, the average pain intensity scores were, respectively, 8.23 and 5.14. Compared to children, more adolescents reported having pain. [28] This suggests that the likelihood of experiencing pain increases with age and with the progression of joint disease in the wake of recurrent bleeding; as a result, in adulthood, a high incidence of discomfort is anticipated.

This study showed that patients with severe pain had higher levels of emotional and psychological distress. It has been suggested that some elements, such as stress and anxiety, affect how painful something is. [29] Another research found a link between current anxiety disorders and pain in the head, shoulders, and back. [30] Distress, rage, and depression are caused by persistent pain. [31]

Hepatitis was present in 37.9% of the patients with hemophilia in the current study. 48% of young adult hemophilia patients had hepatitis and the liver, according to Curtis et al. [32]

Joints, noses, mouth, muscles, and skin were the most frequently bleeding areas in this study. According to Dorgalaleh et al., joint bleeds, nasal bleeds, skin bruising, and dental pain and bleeding were the most common clinical symptoms of hemophilia, which is in line with our findings.[23]

In our study, adult hemophiliac patients' mean HRQoL scores were 51.08 (SD = 19.28). Similar research by Mercan et al. showed that their subjects' mean HRQoL score was 46.3 (SD = 13.1) there. [33] However, patients with hemophilia from Brazil and Greece scored higher on the Haem-A-QoL's QoL scale. [34,35]

The mean HRQoL score of the patients according to another study was 31.1 (12.0). [28]

The HRQoL scores for the SF-12 physical component were also found to be lower than the national average in a different study.[32] Patients must deal with chronic illnesses like hemophilia on a daily basis.[19] They also feel the effects on their psychological health. [36]

The results of the study show, hemophiliacs had the worst HRQoL impairments in "games and recreation," "emotions," and " overall fitness." These findings agreed with those of Mercan et al. and Ferreira et al. [33,34]

The best and worst HRQoL dimensions for patients with hemophilia were "marital life" and "recreation and games," respectively. [35] According to Varaklioti et al., patients with hemophilia had reduced HRQoL, particularly in the area of physical health, and were unable to engage in certain sports and activities. [37] Patients in our study experienced issues with "sports and leisure."

To get patients to exercise, more needs to be done because previous attempts to forbid it have been defeated by granting these patients more access to

factor. [38] Patients benefit physically and socially from this in addition to the former. [39,40]

According to the findings of the current study mild to severe levels of stress, depression, and anxiety were experienced by 45.8%, 58.3%, and 63.5% of the hemophilia patients, respectively. 68% of the patients in Hassan et al.'s study on Egyptian adolescent hemophiliacs experienced mild to severe depression. [14] Other studies, however, found that the prevalence of depression was lower than 37%. [41,42]

Researchers from underdeveloped nations with backgrounds roughly comparable to Iran's have found that patients experience more complications than patients in developed nations, including disability and chronic pain. Anxiety and fear brought on by these problems lead to depression and other psychological problems. [14]

Our study's findings demonstrated that patients with severe pain had lower HRQoL, and that one factor predicting HRQoL was the severity of the pain. According to the same report, pain was linked to a lower HRQoL. [20] Elander et al. also discovered a connection between physical HRQoL and disease severity, pain, and pain acceptance. They thought that accepting pain had an impact on psychological HRQoL as well. [43] Researchers have found a connection between chronic pain and good physical, mental, social, and environmental health in hemophilia patients. A strong link between pain and the severity of the disease was also discovered. [28] Pain affects physical health by affecting bodily mechanics, altering body physics, and impairing sleep. By causing more psychological distress, pain exacerbated psychological issues. By affecting relationships and lowering social activities, it also hurts social interactions. [22] Therefore, pain has an effect on every aspect of HRQoL.

The current study's findings demonstrated that patients' HRQoL improved when they felt less stress, depression, and anxiety. 48 percent of the variation in HRQoL may be attributed to the severity of the predictors' pain and depression. Some hemophiliac patient studies have shown a significant relationship between depression and HRQoL. [15,19] Al-Gamal et al. also mentioned HRQoL in relation to depressive and arousal disorders, and they pointed out that people with chronic illnesses reported experiencing higher levels of psychological stress, which had a detrimental effect on their quality of life. [44]

Due to the limitation of this study's single center design, additional multicenter studies (with larger sample sizes) are suggested to allow for the generalization of the results.

Practical Ramification

Given that hemophiliacs experience significant stress, sadness, and anxiety in addition to HRQoL impairment, the psychological requirements of patients should be considered in to enhance the standard of living quality. It is also advised to conduct additional qualitative research on the HRQoL of patients with hemophilia. Additionally, implementing an intervention to improve HRQoL and minimize stress, anxiety, and sadness in hemophiliacs might be useful.

Conclusion

According to the study's results, about a third of hemophilia patients reported feeling pain, and around most of them reported severe stress, sadness, and distress. The most severe degrees of HRQoL impairment were found to be in the "emotion," "sports and recreation," and "physical performance" Haem-A-QoL components. Additionally, hemophiliacs having better HRQoL showed better pain, anxiety and sadness scores. The degree of discomfort and the prevalence of mild to moderately severe depression symptoms were predictive of the HRQoL in these hemophiliacs. Therefore, proper medical counseling and care lessens the psycho-emotional stress and pain intensity in hemophilia patients to improve their HRQoL. Psychosocial outcomes and patient outcomes would seem to be improved by adding psychology services to the multidisciplinary hemophilia team.

References

1. White GC, Rosendaal F, Aledort LM, Lusher JM, Rothschild C, Ingerslev J. Definitions in hemophilia. Thrombosis and haemostasis. 2001;85(03):560
2. Fischer K, De Kleijn P, Negrier C, Mauser-Bunschoten EP, van der Valk PR, van Galen KP, Willemze A, Schutgens R. The association of haemophilic arthropathy with Health-Related Quality of Life: a post hoc analysis. Haemophilia. 2016 Nov;22(6):833-40.
3. Witkop M, Neff A, Buckner TW, Wang M, Batt K, Kessler CM, Quon D, Boggio L, Recht M, Baumann K, Gut RZ. Self-reported prevalence, description and management of pain in adults with haemophilia: methods, demographics and results from the Pain, Functional Impairment, and Quality of life (P-FiQ) study. Haemophilia. 2017 Jul;23(4):556-65.
4. Roosendaal G, Jansen NW, Schutgens R, Lafeber FP. Haemophilic arthropathy: the importance of the earliest haemarthroses and consequences for treatment. Haemophilia. 2008 Nov;14:4-10.

5. Saulyte Trakymiene S, Clausen N, Poulsen LH, Ingerslev J, Rageliene L. Progression of haemophilic arthropathy in children: a Lithuanian–Danish comparative study. Haemophilia. 2013 Mar;19(2):212-8.
6. Bullinger M, von Mackensen S. Psycho-social determinants of quality of life in children and adolescents with haemophilia—a cross-cultural approach. Clinical psychology & psychotherapy. 2008 May;15(3):164-72.
7. Hartl HK, Reitter S, Eidher U, Ramschak H, Ay C, Pabinger I. The impact of severe haemophilia on the social status and quality of life among Austrian haemophiliacs. Haemophilia. 2008 Jul;14(4):703-8.
8. Solovieva S, Santavirta N, Santavirta S, Konttinen YT. Assessing quality of life in individuals with hereditary blood coagulation disorders. Quality of Life Research. 2004 Jun;13(5):987-1000.
9. Talaulikar D, Shadbolt B, McDonald A, Pidcock M. Health-related quality of life in chronic coagulation disorders. Haemophilia. 2006 Nov;12(6):633-42.
10. Poon JL, Zhou ZY, Doctor JN, Wu J, Ullman MM, Ross C, Riske B, Parish KL, Lou M, Koerper MA, GWADRY-SRIDHAR F. Quality of life in haemophilia A: hemophilia utilization Group Study Va (HUGS-Va). Haemophilia. 2012 Sep;18(5):699-707.
11. Bastani P, Pourmohamadi K, Karimi M. Quality of life in hemophilia complicated by inhibitors. Iranian Red Crescent Medical Journal. 2012 Apr;14(4):250.
12. Handin RI, Lux SE, Stossel TP, editors. Blood: principles and practice of hematology. Lippincott Williams & Wilkins; 2003.
13. Barr RD, Saleh M, Furlong W, Horsman J, Sek J, Pai M, Walker I. Health status and health-related quality of life associated with hemophilia. American journal of hematology. 2002 Nov;71(3):152-60.
14. Hassan TH, Badr MA, Fattah NR, Badawy SM. Assessment of musculoskeletal function and mood in haemophilia A adolescents: a cross-sectional study. Haemophilia. 2011 Jul;17(4):683-8.
15. Siboni SM, Mannucci PM, Gringeri A, Franchini M, Tagliaferri A, Ferretti M, Tradati FC, Santagostino E, Von Mackensen S, Italian Association of Haemophilia Centres (AICE). Health status and quality of life of elderly persons with severe hemophilia born before the advent of modern replacement therapy. Journal of Thrombosis and Haemostasis. 2009 May;7(5):780-6.
16. Witkop M, Guelcher C, Forsyth A, Hawk S, Curtis R, Kelley L, Frick N, Rice M, Rosu G, Cooper DL. Treatment outcomes, quality of life, and impact of hemophilia on young adults (aged 18–30 years) with hemophilia. American journal of hematology. 2015 Dec;90:S3-10.
17. Kodra Y, Cavazza M, Schieppati A, De Santis M, Armeni P, Arcieri R, Calizzani G, Fattore G, Manzoli L, Mantovani L, Taruscio D. The social burden and quality of life of patients with haemophilia in Italy. Blood Transfusion. 2014;12(S3):s567-75.
18. Canclini M, Zanon E, Girolami A. Factors which may influence coping with disease in haemophilia patients. Haemophilia. 2004 Sep;10(5):675-.
19. Rambod M, Sharif F, Molazem Z, Khair K, von Mackensen S. Health-related quality of life and psychological aspects of adults with hemophilia in Iran. Clinical and Applied Thrombosis/Hemostasis. 2018 Oct;24(7):1073-81.
20. Forsyth AL, Witkop M, Lambing A, Garrido C, Dunn S, Cooper DL, Nugent DJ. Associations of quality of life, pain, and self-reported arthritis with age, employment, bleed rate, and utilization of hemophilia treatment center and health care provider services: results in adults with hemophilia in the HERO study. Patient preference and adherence. 2015;9:1549.
21. Rambod M, Sharif F, Molazem Z, Khair K. Pain: the voiceless scream in every haemophilia patient's life. The Journal of Haemophilia Practice. 2016 Jan 25;3(1):8-13.
22. Rambod M, Sharif F, Molazem Z, Khair K. Pain experience in hemophilia patients: a hermeneutic phenomenological study. International journal of community based nursing and midwifery. 2016 Oct;4(4):309.
23. Dorgalaleh A, Dadashizadeh G, Bamedi T. Hemophilia in Iran. Hematology. 2016 May 27;21(5):300-10.
24. Dolatkhah R, Fakhari A, Pezeshki MZ, Shabanlouei R, Tavassoli N, Gholchin M. Social determinants and health-related dimensions of quality of life in adult patients with haemophilia. Haemophilia. 2014 May;20(3):376-81.
25. Ghanizadeh A, Baligh-Jahromi P. Depression, anxiety and suicidal behaviour in children and adolescents with Haemophilia. Haemophilia. 2009 Mar;15(2):528-32.
26. Holstein K, Klamroth R, Richards M, Carvalho M, PÉREZ-GARRIDO R, Gringeri A, European Haemophilia Therapy Standardization Board. Pain management in patients with haemophilia: a European survey. Haemophilia. 2012 Sep;18(5):743-52.
27. Curtis R, Baker J, Riske B, Ullman M, Niu X, Norton K, Lou M, Nichol MB. Young adults with hemophilia in the US: demographics, comorbidities, and health status. American journal of hematology. 2015 Dec;90:S11-6.
28. Rambod M, Forsyth K, Sharif F, Khair K. Assessment and management of pain in children and adolescents with bleeding disorders: a cross-sectional study from three haemophilia centres. Haemophilia. 2016 Jan;22(1):65-71.
29. Auerswald G, Dolan G, Duffy A, Hermans C, Jiménez-Yuste V, Ljung R, Morfini M, Lambert T, Šalek SZ. Pain and pain management in haemophilia. Blood Coagulation & Fibrinolysis. 2016 Dec;27(8):845.
30. Williams LJ, Pasco JA, Jacka FN, Dodd S, Berk M. Pain and the relationship with mood and anxiety disorders and psychological symptoms. Journal of psychosomatic research. 2012 Jun 1;72(6):452-6.
31. Dersh J, Polatin PB, Gatchel RJ. Chronic pain and psychopathology: research findings and theoretical considerations. Psychosomatic medicine. 2002 Sep 1;64(5):773-86.
32. Curtis R, Baker J, Riske B, Ullman M, Niu X, Norton K, Lou M, Nichol MB. Young adults with hemophilia in the US: demographics, comorbidities, and health status. American journal of hematology. 2015 Dec;90:S11-6.
33. Mercan A, Sarper N, Inanır M, Mercan HI, Zengin E, Kılıç SC, Gökalp AS. Hemophilia-Specific Quality of Life Index (Haemo-QoL and Haem-A-QoL questionnaires) of children and adults: result of a single center from Turkey. Pediatric hematology and oncology. 2010 Aug 27;27(6):449-61.
34. Ferreira AA, Leite IC, Bustamante-Teixeira MT, Corrêa CS, Cruz DT, Rodrigues DD, Ferreira MC. Health-related quality of life in hemophilia: results of the Hemophilia-Specific Quality of Life Index (Haem-a-Qol) at a Brazilian blood center. Revista Brasileira de Hematologia e Hemoterapia. 2013;35:314-8.
35. Varaklioti A, Kontodimopoulos N, Katsarou O, Niakas D. Psychometric properties of the Greek Haem-A-QoL for measuring quality of life in Greek haemophilia patients. BioMed Research International. 2014 Jan 1;2014.
36. Von Mackensen S, Eldar-Lissai A, Auguste P, Krishnan S, Von Maltzahn R, Yu R, Wyrwich KW. Measurement properties of the Haem-A-QoL in haemophilia clinical trials. Haemophilia. 2017 May;23(3):383-91.

37. Varaklioti A, Kontodimopoulos N, Niakas D, Kouramba A, Katsarou O. Health-related quality of life and association with arthropathy in Greek patients with hemophilia. Clinical and Applied Thrombosis/Hemostasis. 2018 Jul;24(5):815-21.
38. Weigel N, Carlson BR. Physical activity and the hemophiliac: yes or no?. American corrective therapy journal. 1975;29(6):197-205.
39. Von Mackensen S. Quality of life and sports activities in patients with haemophilia. Haemophilia. 2007 Sep;13:38-43.
40. Buzzard BM. Physiotherapy, rehabilitation and sports in countries with limited replacement coagulation factor supply. Haemophilia. 2007 Sep;13:44-6.
41. Logan FA, Maclean A, Howie CA, Gibson B, Hann IM, Parry-Jones WL. Psychological disturbance in children with haemophilia. British medical journal. 1990 Dec 1;301(6763):1253-6.
42. Khatwa SA, Abdou MH. Adult depression in Alexandria, Egypt, 1998. The Journal of the Egyptian Public Health Association. 1999 Jan 1;74(3-4):333-52.
43. Elander J, Morris J, Robinson G. Pain coping and acceptance as longitudinal predictors of health-related quality of life among people with haemophilia-related joint pain. European Journal of Pain. 2013 Jul;17(6):929-38.
44. Al-Gamal E. Quality of life, anxiety and depression among patients with chronic obstructive pulmonary disease and their spouses. Issues in mental health nursing. 2014 Oct 1;35(10):761-7.