



ORIGINAL ARTICLE

Evaluation of Quality of Life in Children with Hemophilia

Hemofili Nedeni İle Takip Edilen Hastaların Yaşam Kalite Standartlarının Değerlendirilmesi

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ABSTRACT

Aim: Hemophilia is an X-linked hereditary coagulation disorder characterized by recurrent bleeding episodes that significantly impair patients' quality of life. This study aimed to evaluate the quality of life levels of pediatric patients with hemophilia and their parents according to clinical variables such as disease severity, prophylaxis status, and the presence of target joints.

Materials and Methods: A total of 40 hemophilia patients aged 8-12 years and their parents were included in this cross-sectional study. Data were collected using the Pediatric Quality of Life Inventory (PedsQL™) Hematology/Oncology Module. The form included 27 questions covering domains such as pain and hurt, nausea, procedural concern, treatment concern, anxiety, cognitive problems, perceived physical appearance, and communication.

Results: Of the patients included in our study, 23 (57.5%) were being followed up for severe hemophilia. While 24 (60%) patients were receiving regular prophylaxis, 3 (7.5%) were inhibitor-positive. Thirteen patients (32.5%) had target joint damage. The prophylaxis (+) group reported significantly less pain and hurt than the non-prophylaxis (-) group ($p=0.038$). Similarly, the group without target joints (target joint -) had significantly better scores for pain and hurt than the group with target joints (target joint +) ($p=0.025$). In the comparison based on disease severity, patients with severe hemophilia experienced significantly more pain than those with mild or moderate forms ($p<0.001$).

Conclusions: Our findings indicate that the most significant problems adversely affecting the quality of life of children with hemophilia are frequent hospitalizations, recurrent treatment needs, joint damage, and consequent pain. Our results strongly support that the prevention of joint damage should be a primary goal to improve quality of life. We conclude that early diagnosis, effective and individualized treatment, and regular prophylaxis can prevent these adverse outcomes and enhance patients' living standards.

Keywords: Child, hemophilia, joint health, PedsQL™, prophylaxis, quality of life.

ÖZ

Amaç: Hemofili, hastaların yaşam kalitesini önemli ölçüde etkileyen tekrarlayan kanama atakları ile karakterize, X'e bağlı kalıtsal bir koagülasyon bozukluğudur. Bu çalışmada, hemofili tanısıyla takip edilen pediatrik hastaların ve ebeveynlerinin yaşam kalitesi düzeylerinin hastalık şiddeti, profilaksi durumu ve hedef eklem varlığı gibi klinik değişkenlere göre değerlendirilmesi amaçlanmıştır.

Gereç ve Yöntemler: Çalışmaya 8-12 yaş aralığında 40 hemofili hastası ve ebeveynleri dahil edilmiştir. Bu kesitsel çalışmada veriler, Pediatrik Yaşam Kalitesi Envanteri (PedsQL) Hematoloji/Onkoloji Modülü kullanılarak toplanmıştır. Bu form, ağrı ve acı, bulantı, işlemsel kaygı, tedavi kaygısı, endişe, bilişsel sorunlar, algılanan fiziksel görünüm ve iletişim alanlarını kapsayan 27 sorudan oluşmaktadır.

Bulgular: Çalışmaya katılan hastaların 23'ü (%57,5) ağır hemofili tanısı ile izlenmekteydi. Hastaların 24'ü (%60) düzenli profilaksi tedavisi alırken, 3'ünde (%7,5) inhibitör saptanmıştır. On üç hastada (%32,5) hedef eklem hasarı mevcuttu. Profilaksi alan grubun (profilaksi +), almayan gruba (profilaksi -) kıyasla istatistiksel olarak anlamlı düzeyde daha az ağrı ve acı bildirdiği görülmüştür ($p=0.038$). Benzer şekilde, hedef eklem hasarı olmayan grubun (hedef eklem -) ağrı ve acı skorları, hedef eklem hasarı olan gruba (hedef eklem +) göre anlamlı derecede daha iyi bulunmuştur ($p=0.025$). Hastalığın şiddetine göre yapılan karşılaştırmada ise ağır tip hemofili hastalarının, orta ve hafif tiplere göre anlamlı olarak daha fazla ağrı ve acı yaşadığı tespit edilmiştir ($p<0.001$).

Sonuçlar: Çalışmamız, hemofili hastası çocuklarda yaşam kalitesini olumsuz etkileyen temel faktörlerin sık hastaneye yatış, tekrarlayan tedavi gereksinimi, hastalık şiddeti, hedef eklem varlığı ve buna bağlı gelişen kronik ağrı olduğunu ortaya koymuştur. Bulgularımız, eklem sağlığının korunmasının yaşam kalitesini artırmada öncelikli bir hedef olması gerektiğini güçlü bir şekilde desteklemektedir. Etkin ve kişiselleştirilmiş profilaksi uygulamasının bu olumsuzlukları önleyebileceği ve hastaların yaşam standartlarını yükseltebileceği kanaatindeyiz.

Anahtar Kelimeler: Eklem sağlığı, Hemofili, çocuk, PedsQL, profilaksi, yaşam kalitesi.

Introduction

Hemophilia is an X-linked hereditary coagulation disorder in which males exhibit clinical signs and symptoms, while females are typically carriers [1]. The most debilitating problem for patients with hemophilia is recurrent bleeding episodes. Bleeding, especially into the musculoskeletal system, can begin as early as the months when patients start to crawl. Recurrent hemorrhages, which frequently occur in weight-bearing joints, lead to pain and swelling, which in turn cause progressive joint damage (hemophilic arthropathy) and decreased range of motion. Consequently, children may be unable to perform the same movements as their peers, avoid playing games due to the risk of trauma, and become isolated from sports activities [2].

Over the past decades, significant advances in the follow-up and treatment of hemophilia have not only prolonged life expectancy but have also shifted the focus towards preventing long-term complications and improving Health-Related Quality of Life (HRQoL) [3]. HRQoL is defined as the patient's perception of the effect of the disease and its treatment on their daily life and well-being [4,5]. Standardized scales are crucial tools to measure HRQoL, enabling objective and comparable data collection [6]. Recent systematic reviews have highlighted the positive impact of prophylaxis on HRQoL and established that joint health is a key determinant of quality of life [6].

In our study, we aimed to evaluate the quality of life standards of mild, moderate, and severe hemophilia patients with varying clinical characteristics (inhibitor status, presence of target joints, and prophylaxis regimen) and their parents by using a validated quality of life assessment inventory.

Materials and Methods

A total of 40 hemophilia patients aged 8–12 years and their parents, who were followed up at the Pediatric Hematology Outpatient Clinic of Kanuni Sultan Süleyman Training and Research Hospital, were included in this study. Patients were evaluated after approval was obtained from the Ethics Committee (Decision No: 16439, Date: 11.09.2014). The study was conducted under the principles of the Declaration of Helsinki. This research is based on a doctoral thesis completed in 2015, and the data reflect the clinical status and treatment standards of that period. Due to the specific pediatric population and single-center nature, a formal power analysis was not performed, and the sample size remains limited, which should be considered when generalizing the results.

Detailed information about the survey was given to the patients and their families participating in the study, and written informed consent was obtained from all participants. The study was planned and implemented as a cross-sectional analysis. Patients and their parents were interviewed face-to-face, and data were collected using the PedsQL™ Quality of Life Inventory Cancer Module's Child and Parent Forms [7]. This module was preferred because it includes specific domains such as "Pain and Hurt" and "Treatment Concern," which are more representative of the clinical burden of hemophilia than generic scales. Its validity in chronic hematological disorders

has been previously demonstrated [8,9].

The inventories assess eight domains: 1) Pain and Hurt, 2) Nausea, 3) Procedural Concern, 4) Treatment Concern, 5) Anxiety, 6) Cognitive Problems, 7) Perceived Physical Appearance, and 8) Communication, through 27 multifaceted questions. Responses were scored using a five-point Likert scale: 0 (Never a problem), 1 (Almost never a problem), 2 (Sometimes a problem), 3 (Often a problem), and 4 (Almost always a problem). For analysis, scores were linearly transformed to a 0–100 scale, where higher scores indicate a better HRQoL.

Patients with a factor level <1% were classified as severe, 1–5% as moderate, and >5–40% as mild hemophilia, in line with established international guidelines [1]. Patients were categorized based on whether they received on-demand factor therapy or regular prophylaxis. Data on age, annual bleeding rate, presence of target joints, prophylaxis status, and factor levels were collected.

Statistical Analysis: Data were analyzed using SPSS (Statistical Package for Social Sciences) for Windows, version 22.0. Descriptive statistical methods were used to evaluate the study data. The Mann-Whitney U test and Kruskal-Wallis test were used for group comparisons. For post-hoc analysis following the Kruskal-Wallis test, the Dunn-Bonferroni test was utilized to identify significant differences between groups while controlling for Type I error. The potential for Type I errors due to multiple comparisons is acknowledged as a methodological consideration. Results were evaluated at a 95% confidence interval, and a p-value of ≤0.05 was considered significant.

Results

Forty patients and their parents were included in our study. Of the patients, 23 (57.5%) had severe, 11 (27.5%) had moderate, and 6 (15%) had mild hemophilia. Sixty percent of the patients were receiving regular prophylaxis, while 40% were not. Regarding inhibitor status, 7.5% of patients were inhibitor-positive (+), and 92.5% were inhibitor-negative (-). All three inhibitor-positive patients were classified as having severe hemophilia with a high frequency of breakthrough bleeds. Thirteen (32.5%) patients had target joint damage, whereas 27 (67.5%) did not (Figure 1).

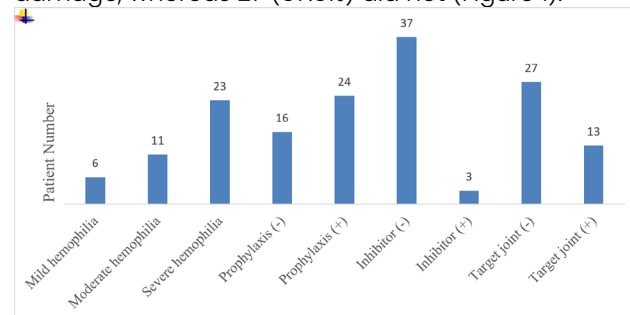


Figure 1. Distribution of hemophilia patients in the 8–12 age group who participated in the study

In the pediatric group, the mean pain and hurt score of the prophylaxis (+) group was statistically significantly better than the non-prophylaxis (-) group ($p=0.038$), but their mean communication score

was significantly worse ($p=0.002$). No statistically significant difference was observed between the groups for other parameters. In the parent group, only the mean communication score of the prophylaxis (+) group was statistically significantly worse than the prophylaxis (-) group ($p=0.046$) (Table 1).

When comparing groups based on inhibitor status, the inhibitor (+) pediatric group had significantly worse scores in procedural concern, treatment concern, and cognitive problem parameters than the inhibitor (-) group ($p=0.039$, $p=0.027$, and $p=0.041$, respectively). No significant difference was found between the parent groups (Table 2).

Table 1. Evaluation of quality of life parameters of children and parent groups according to prophylaxis status

	Prophylaxis (-) n:16		Prophylaxis (+) n:24		p value	
	Patient	Parent	Patient	Parent	Patient	Parent
Pain and hurt	69,53±18,80	58,59±26,11	57,29±16,86	45,83±20,08	0.038	0.089
Nausea	82,81±12,64	81,88±17,69	89,79±10,18	88,54±13,47	0.079	0.184
Procedural concern	70,3±25,81	53,65±15,21	81,25±10	59,03±35,18	0.140	0.568
Treatment concern	86,46±10,21	55,21±29,17	93,4±6,03	67,71±39,42	0.167	0.285
Anxiety	71,35±19,95	61,46±31,6	79,51±14,53	66,32±31,32	0.142	0.635
Cognitive problems	64,38±25,16	51,56±32,59	68,33±21,25	64,79±24,78	0.595	0.153
Perceived physical appearance	60,94±22,09	66,67±22,57	69,79±19,94	73,61±23,14	0.195	0.354
Communication	61,98±23,17	58,85±23,86	84,72±19,14	75,35±25,36	0.002	0.046

Table 2. Evaluation of quality of life parameters of patient and parent groups according to inhibitor status

	Inhibitor (-) n:37		Inhibitor (+) n:3		p value	
	Patient	Parent	Patient	Parent	Patient	Parent
Pain and hurt	63,18±18,15	51,35±24,08	50±21,65	45,83±7,22	0.239	0.698
Nausea	87,3±12,28	84,08±10,28	83,33±15,28	83,33±10,82	0.599	0.771
Procedural concern	77,25±23,29	58,56±28,29	90,22±9,25	36,11±31,55	0.039	0.197
Treatment concern	80,09±8,94	63,29±25,38	94,22±4,81	55,56±38,83	0.027	0.724
Anxiety	76,8±17,03	64,19±21,97	69,44±20,97	66,67±22,05	0.482	0.897
Cognitive problems	67,3±12,04	60,54±28,55	82±9,14	46,67±30,55	0.041	0.425
Perceived physical appearance	66,67±21,7	72,97±11,64	61,11±9,62	64,44±15,46	0.665	0.210
Communication	73,65±23,28	66,44±15,42	88,96±8,65	67,12±4,81	0.096	0.865

When the groups were compared based on the presence of a target joint, the mean scores for pain and hurt and perceived physical appearance in the pediatric group with a target joint were statistically significantly worse than the group without a target joint ($p=0.025$ and $p=0.019$, respectively). In the parent group, the mean scores for pain and hurt, procedural concern, treatment concern and perceived physical appearance were also statistically significantly worse in the target joint (+) group ($p=0.009$, $p=0.004$, $p=0.007$, and $p=0.04$, respectively) (Table 3).

Finally, when evaluating quality of life parameters among disease severity groups using the Dunn-Bonferroni test for post-hoc analysis, a significant difference was found between the mild and moderate groups in terms of anxiety scores, with the mild hemophilia group experiencing fewer anxiety problems ($p=0.049$). In comparisons involving the severe group (mild-severe and moderate-severe), the severe hemophilia group experienced more problems across all parameters, with significantly worse mean scores (Table 4).

Table 3. Evaluation of quality of life parameters of patient and parent groups according to target joint status

	Target joint (-) n:27		Target joint (+) n:13		p value	
	Patient	Parent	Patient	Parent	Patient	Parent
Pain and hurt	52,88±16,26	51,35±24,08	66,67±18,01	45,83±7,22	0.025	0.009
Nausea	87,59±10,32	84,08±10,28	85,77±16,18	83,33±10,82	0.667	0.204
Procedural concern	73,77±22,01	58,56±28,29	83,33±14,06	36,11±31,55	0.219	0.004
Treatment concern	90,12±6,02	63,29±25,38	91,67±4,83	55,56±38,83	0.772	0.007
Anxiety	78,09±17,62	64,19±21,97	72,44±14,41	66,67±22,05	0.335	0.401
Cognitive problems	66,3±26	60,54±28,55	67,69±14,23	46,67±30,55	0.858	0.697
Perceived physical appearance	55,04±22,57	72,97±11,64	75±14,43	64,44±15,46	0.019	0.006
Communication	75±23,8	66,44±15,42	76,92±21,61	67,12±4,81	0.812	0.768

Table 4. Comparison of quality of life parameters of patient groups according to mild-moderate-severe hemophilia status (Post-hoc: Dunn-Bonferroni)

Dunn-Bonferroni test	Pain and hurt (p)	Anxiety (p)	Cognitive problems (p)	Communication (p)
Mild / Moderate	0.257	0.049	0.604	0.587
Mild / Severe	0.001	0.007	0.023	0.001
Moderate / Severe	0.009	0.023	0.032	0.001

Discussion

Hemophilia is an inherited blood disorder that results in impaired bleeding control due to deficiencies in coagulation factors. The most significant problem for these patients is recurrent bleeding episodes. The fear of bleeding from childhood and chronic joint problems lead these patients to live a sedentary life [2, 10, 11].

In our study, when we compared the prophylaxis (+) group, who received factor replacement 2 to 3 times a week, with the prophylaxis (-) group, who received on-demand treatment, individuals in the prophylaxis (+) group reported less pain and hurt. This is primarily because individuals receiving prophylaxis experience less joint and muscle bleeding and thus have better joint health. This finding is consistent with the extensive body of evidence demonstrating that prophylaxis improves HRQoL and is now considered the standard of care [6, 12].

On the other hand, the prophylaxis (+) group visits the hospital more frequently for regular infusions, which may lead to more disruptions in their school and social lives. In our study, communication problems were more common in the prophylaxis (+) group ($p=0.002$). This may be attributed to the rigorous schedule of infusions, which requires frequent medical interactions and can lead to “treatment fatigue,” potentially affecting the child’s perception of social communication and autonomy. Furthermore, recent literature suggests that while prophylaxis improves physical scores, the psychological burden on parents and children can differ significantly; parents often perceive a higher burden of treatment than the children themselves [13, 14].

When we analyzed our patients for the presence of inhibitors, only 3 patients were inhibitor (+). Although this small number precludes statistically significant conclusions, the inhibitor (+) group had worse scores for procedural concern, treatment concern, and cognitive problems. This was thought to be related to the fact that the inhibitor (+) group has more difficult disease control and more treatment-related challenges. In our study, it is noteworthy that all inhibitor-positive patients were classified as having severe hemophilia with a high frequency of breakthrough bleeds. The clinical management of inhibitors in severe cases is significantly more complex, often requiring more frequent medical interventions and specialized therapies, which likely explains the increased treatment-related anxiety and lower HRQoL scores observed in this subgroup. Recent studies show that novel agents, such as emicizumab, provide effective bleed control in patients with inhibitors, leading to significant improvements in the quality of life for both patients and their parents [15].

Regarding the presence of target joints, the pain and hurt score of the target joint (+) group was significantly worse than the target joint (-) group. The presence of a target joint causes both limitation of movement and local inflammation and pain. The results of our study show that joint damage is an important cause of pain and suffering. This finding aligns with numerous studies that report joint health as the most important variable for physical HRQoL [12,16]. The target joint (+) group also had a worse perceived physical appearance score, which may be attributed to the deformities that occur in the target joints and the individuals’ discomfort. A study by Wu et al. also found that joint pain was the most important factor affecting physical health and that chronic pain was closely related to psychosocial health [16].

When comparing disease severity, significant differences were found in pain and hurt, anxiety, cognitive problems, and communication scores, with outcomes worsening as severity increased. This is closely related to the increased number of bleeds and joint damage in severe hemophilia. The literature consistently shows that quality of life scores decrease as the severity of the disease increases and joint health deteriorates [17,18].

Although our study focuses on pediatric patients, the burden of hemophilia across the lifespan in Turkey is significant. Arslan Davulcu et al. highlighted that even in cases of acquired hemophilia in adults, early diagnosis and management of complications are vital for survival and quality of life. While congenital and acquired hemophilia differ in etiology, the necessity of a multidisciplinary approach and the impact of the disease on the Turkish healthcare system remain a common theme [19].

Limitations of the Study: The most important limitations of our study include the limited sample size, particularly the very small number of inhibitor-positive patients ($n=3$), and the fact that the data set is from 2015. These factors limit the statistical power and the generalizability of our findings to the current era of novel non-factor therapies.

Conclusions

In our study, the most important problems affecting the quality of life of patients with hemophilia were found to be frequent hospitalization, recurrent treatment needs, joint damage, and consequently, pain. The management of hemophilia requires a multidisciplinary approach, and the combination of early diagnosis, close follow-up, and individualized treatment has become the gold standard. Our findings emphasize that proactive strategies, particularly those aimed at preserving joint health and providing effective prophylactic treatment, are critical to improving the physical, social, and

psychological well-being of this patient population.

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References

1. Srivastava A, Brewer AK, Mauser-Bunschoten EP, Key NS, Kitchen S, Llinas A, et al. Treatment Guidelines Working Group on Behalf of The World Federation Of Hemophilia. Guidelines for the management of hemophilia. *Haemophilia*. 2013;19(1):e1-47. Epub 2012 Jul 6. PMID: 22776238
2. Aznar JA, Magallón M, Querol F, Gorina E, Tusell JM. The orthopaedic status of severe haemophiliacs in Spain. *Haemophilia*. 2000;6(3):170-6. PMID: 10792475.
3. Fischer K, Grobbee DE, van den Berg HM. RCTs and observational studies to determine the effect of prophylaxis in severe haemophilia. *Haemophilia*. 2007;13(4):345-50. PMID: 17610546.
4. Bullinger M, von Mackensen S, Fischer K, Khair K, Petersen C, Ravens-Sieberer U, et al. Pilot testing of the 'Haemo-QoL' quality of life questionnaire for haemophiliac children in six European countries. *Haemophilia*. 2002;8 Suppl 2:47-54. PMID: 11966854.
5. Trippoli S, Vaiani M, Linari S, Longo G, Morfini M, Messori A. Multivariate analysis of factors influencing quality of life and utility in patients with haemophilia. *Haematologica*. 2001;86(7):722-8. PMID: 11454527.
6. Oladapo AO, Epstein JD, Williams E, Ito D, Gringeri A, Valentino LA. Health-related quality of life assessment in haemophilia patients on prophylaxis therapy: a systematic review of results from prospective clinical trials. *Haemophilia*. 2015;21(5):e344-58. Epub 2015 Jul 17. PMID: 26390060.
7. Varni JW, Burwinkle TM, Katz ER, Meeske K, Dickinson P. The PedsQL in pediatric cancer: reliability and validity of the Pediatric Quality of Life Inventory Generic Core Scales, Multidimensional Fatigue Scale, and Cancer Module. *Cancer*. 2002;94(7):2090-106. PMID: 11932914.
8. Kürtüncü Tanır M, Kuşuoğlu S. Pediatrik yaşam kalitesi envanteri (PedsQL) sağlık bakım memnuniyeti hematoloji/onkoloji modülü ebeveyn formu geçerlik-güvenirliliği. *ASHD*. 2012;11(2):13-23.
9. Yıldız Kabak V, Yakut Y, Çetin M, Düğer T. Reliability and Validity of the Turkish Version of the PedsQL 3.0 Cancer Module for 2- to 7-Year-Old and the PedsQL 4.0 Generic Core Scales for 5- to 7-Year-Old: The Hacettepe University Experience. *Türk J Hematol*. 2016;33(3):236-43. Epub 2016 Apr 18. PMID: 27095607; PMCID: PMC5111470.
10. Álvarez-Vera JL, Anaya-Cuellar I, Arana-Luna LL, Ávila-Castro D, Bates-Martín RA, Cesarman-Maus G, et al. Consensus on hemophilia in Mexico. *Gac Med Mex*. 2021;157(Supl 1):S1-S37. English. PMID: 33588427.
11. Türk Hematoloji Derneği. Ulusal Hemofili Tanı ve Tedavi Kılavuzu. 2021
12. Azeredo-da-Silva AF, Zanotto BS, Kuwabara YS, Mata VE. Quality of life in children and adolescents with hemophilia A: A systematic review and meta-analysis. *Res Pract Thromb Haemost*. 2022;7(1):100008. PMID: 36970745; PMCID: PMC10031335.
13. Chowdary P, Ofori-Asenso R, Nissen F, et al. Disease Burden, Clinical Outcomes, and Quality of Life in People with Hemophilia A without Inhibitors in Europe: Analyses from CHES II/CHES PAEDs. *TH Open*. 2024;8(2):e181-e193.
14. Benemei S, Boni L, Castaman G. Outcome measures in hemophilia: current and future perspectives. *Expert Rev Hematol*. 2024;17(7):329-340.
15. Mancuso ME, Mahlangu J, Sidonio R Jr, Trask P, Uguen M, Chang T, et al. Health-related quality of life and caregiver burden of emicizumab in children with haemophilia A and factor VIII inhibitors-Results from the HAVEN 2 study. *Haemophilia*. 2020;26(6):1009-1018.
16. Wu J, Lou M, Riske B, Ullman M, Baker J, Curtis R. Impact of pain on health-related quality of life in persons with hemophilia from the hemophilia utilization group studies part VI (HUGS VI): USA experience. *Haemophilia*. 2018;24:176.
17. Poon JL, Doctor JN, Nichol MB. Longitudinal changes in health-related quality of life for chronic diseases: an example in hemophilia A. *J Gen Intern Med*. 2014;29 Suppl 3(Suppl 3):S760-6.
18. Srivastava A, Santagostino E, Dougall A, Kitchen S, Sutherland M, Pipe SW, et al. WFH Guidelines for the Management of Hemophilia panelists and co-authors. WFH Guidelines for the Management of Hemophilia, 3rd edition. *Haemophilia*. 2020;26 Suppl 6:1-158.
19. Arslan Davulcu E, Demirci Z, Yılmaz U, et al. Acquired Hemophilia A In Adults: A Multicenter Study from Turkey. *Indian J Hematol Blood Transfus*. 2023;39(1):107-115.