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Original Article

Hemophilia and Obesity: Evaluating Prophylactic Dosing and Treatment Outcomes

Hemofili ve Obezite: Profilaktik Doz ve Tedavi Sonuçlarının Değerlendirilmesi

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ABSTRACT

Objective: Advancements in the treatment of hemophilia have extended life expectancy of the patients, while leading to the emergence of new comorbidities, including obesity, among them. This study aimed to evaluate the prevalence of obesity and overweight in patients with hemophilia while examining their associations with the clinical characteristics of the disease.

Method: Hemophilia patients were included in this single-center cross-sectional study. To assess joint health and functionality, the Functional Independence Score in Hemophilia and the Hemophilia Joint Health Score (HJHS) were applied. Patients were grouped according to their body mass indexes (BMIs). Differences in the number of bleeding episodes, prophylactic doses, and joint scores among BMI groups were evaluated.

Results: A total of 35 hemophilia patients aged between 4 and 20 years were included in the study. Based on their BMIs, 8 patients (22.9%) were obese, and 11 patients (31.4%) were obese/overweight. Patients in the obese/overweight group were significantly younger than those in the other group. No significant difference was found between the groups in terms of annual bleeding episodes and HJHS. Interestingly, although obese/overweight patients received significantly lower prophylaxis doses per kilogram of body weight, did not show any difference in clinical scores.

Conclusions: Our findings suggest that dose adjustments based on ideal body weight may lead to similar treatment outcomes. Additionally, younger age and parental protective behaviors may contribute to occurrence of fewer bleeding episodes in obese/overweight patients.

Keywords: Bleeding, hemophilia, obesity, overweight

ÖZ

Amaç: Hemofili tedavisindeki gelişmeler yaşam süresini uzatmış ve hastalar arasında obezite de dahil olmak üzere yeni komorbiditelerin ortaya çıkmasına neden olmuştur. Bu çalışmanın amacı hemofili hastalarında obezite ve fazla kilolu sıklığını tespit etmek ve bunun hemofilinin klinik özellikleriyle ilişkisini araştırmaktır.

Yöntem: Bu tek merkezli kesitsel çalışmaya hemofili hastaları dahil edildi. Eklem sağlığı ve işlevselliğini değerlendirmek amacıyla Hemofilide Fonksiyonel Bağımsızlık Skoru ve Hemofili Eklem Sağlığı Skoru uygulandı. Hastalar, vücut kitle indeksine göre gruplandırıldı. Vücut kitle indeksi grupları arasında kanama sayıları, profilaksi dozları ve eklem skorlamaları açısından fark olup olmadığı değerlendirildi.

Bulgular: Çalışmaya yaşları 4 ile 20 arasında değişen toplam 35 hemofili hastası dahil edildi. Vücut kitle indeksine göre 8 hasta (%22,9) obez, 11 hasta (%31,4) obez/fazla kilolu olarak sınıflandırıldı. Obez/fazla kilolu gruptaki hastalar, diğer gruptakilere göre anlamlı olarak daha küçük yaştaydı. Yıllık kanama sayıları ve Hemofili Eklem Sağlığı Skoru açısından gruplar arasında anlamlı bir fark bulunmadı. İlginç bir şekilde, vücut ağırlığının kilogramı başına anlamlı olarak daha düşük profilaksi dozları almalarına rağmen, obez/fazla kilolu hastalar klinik skorlarda herhangi bir farklılık göstermedi.

Sonuç: Bulgularımız, ideal vücut ağırlığına dayalı doz ayarlamalarının benzer tedavi sonuçlarına yol açabileceğini göstermektedir. Ayrıca, daha küçük yaşta olmak ve ebeveynlerin koruyucu tutumları, obez ya da fazla kilolu hastalarda daha az sayıda kanama epizodu görülmesine katkıda bulunmuş olabilir.

Anahtar kelimeler: Kanama, hemofili, obezite, fazla kilolu

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INTRODUCTION

Hemophilia is a bleeding disorder caused by inadequate synthesis of clotting factors. It is estimated to affect 400,000 people worldwide and is characterized by easy bleeding, delayed clotting, and intra-articular bleeding[1]. Patients may feel symptoms of joint bleeding such as swelling, pain, increased heat, and tingling on the affected site. With recurrent bleeding episodes, synovial damage develops and permanent damage occurs in the joint. Morbidity in hemophilia is often defined in terms of musculoskeletal dysfunction, while its severity is determined by clinical and radiological joint scores[2].

Based on their bleeding profile, patients with severe, and some with moderate hemophilia receive regular prophylaxis. Early initiation of primary prophylaxis is the most important tool in preserving joint function and preventing recurrent bleeding episodes[3]. Thanks to patients' access to factor concentrates and regular prophylactic treatment, the episodes of joint bleeding and the incidence of arthropathy have decreased dramatically[4].

Advancements in the management of hemophilia have increased life expectancy, however new morbidities have emerged among patients. In recent studies, the prevalence of obesity in hemophilia patients has increased up to the incidence rates observed in the general population, while some have reported obesity rates higher than those seen in the general population[5-8]. Some studies have found that hemophilic arthropathy is more common in obese hemophilia patients and that there is a correlation between increased body mass index (BMI) and decreased range of motion (ROM) of the joints[6,9,10]. In this context, obesity further increases the disease burden for patients whose movements are already restricted due to muscle dysfunction and joint inflammation. Additionally, some studies have shown that obesity is associated with an increased number of bleeding episodes[6,11]. However, consistent evidence has not yet been presented that weight gain in hemophilia patients creates a tendency to bleed, and there are studies that claim the opposite[12].

The objectives of this study were to determine the physical performance of hemophilia patients followed up in a tertiary care hospital in Turkey using objective criteria, to investigate the prevalence of obesity/overweight and its association with clinical features of hemophilia in these patients.

MATERIALS and METHODS

A single-center cross-sectional study was conducted at a tertiary care hospital, which is a referral center for the treatment of pediatric patients in the Aegean region of Turkey. Approval of the Local Research Ethics Committee of University of Health Sciences Türkiye, Dr. Behçet Uz Pediatric Diseases and Surgery Training and Research Hospital (approval number: 2021/03-09 dated: 11.02.2021) and written informed consent were obtained from the parents of the patients. Patients with hemophilia A and B between the ages of 4 and 20 years who applied to the Pediatric Hematology Clinic of Dr. Behçet Uz Children's Hospital for routine follow-up between February 2021 and March 2021 were included in this study. Patients who had bleeding episodes (joint, soft tissue, etc.) in the last two weeks or who were inhibitor-positive hemophilia were excluded from the study.

Age, type of hemophilia, clinical classification, the dose of prophylactic treatment (if any), the presence, and number of affected target joint(s), and extra-articular bleeding in the last six months/year were recorded on the case report form. The Functional Independence Score in Hemophilia (FISH) was applied to cases aged 7 years and older. The Hemophilia Joint Health Score (HJHS) v 2.1 was applied to all cases by a physical therapy and rehabilitation specialist. Body weights, and heights of the cases were measured, and their BMIs were calculated during outpatient clinic visits. For patients under 18 years of age, the BMI percentile reference values updated for Turkish children by Neyzi et al.[13] in 2015 were used. Patients over the age of 18 years were classified according to BMI without using percentiles and recorded in the case report form.

Definitions Used in the Study

Type of Hemophilia

Hemophilia patients with Factor (F) VIII deficiency are called hemophilia A, and those with FIX deficiency hemophilia B.

Clinical Classification of Hemophilia

Hemophilia patients with a basal factor level of <1% are classified as severe hemophilia, 1-5% as moderate hemophilia, and 5-40% as mild hemophilia.

Presence of Inhibitor

Inhibitor titer of >0.6 Bethesda Units (BU)/mL for FVIII; >0.3 BU/mL for FIX is considered inhibitor positive.

Prophylaxis

Even in the absence of acute bleeding episodes, factor concentrates are administered to patients regularly once, twice or three times a week to prevent complications of the disease.

Target Joint

The joint that demonstrates three or more episodes of intraarticular bleedings within 6 months is called a target joint.

BMI

Calculated by dividing body mass in kilograms by the square of height in meters.

Classification by BMI

When classifying BMI in the pediatric population, BMI percentiles are used according to the age and gender of the population. Accordingly; pediatric patients with BMIs under 5 percentile are classified as underweight, 5-85 percentile as normal, 85-95 percentile as overweight, 95 percentile and above as obese. Adult patients with BMIs below 18.5 are classified as underweight, 18.5-24.9 as normal, 25.0-29.9 as overweight, and 30 and above as obese.

Joint Health Scoring Systems Used in the Study

HJHS

The current version of the scale, HJHS v 2.1, allows the evaluation of six joints (right and left knee, elbow, and ankle) based on eight items[14]. These items are joint swelling (0-3 points), duration of swelling (0-1), muscle atrophy (0-2), crepitation with movement (0-2), loss of flexion (0-3), loss of extension (0-3), joint pain (0-2), and strength (0-4). The global gait score is evaluated between 0-4 points, with 1 point for each of the skills of walking, climbing stairs, running, and jumping on one leg. Each joint can receive a score between 0-20. The scores from each joint are summed, and the global gait score is added. The maximum score is 124, and the higher the score, the worse the joint health. Cases with a score of zero are considered healthy according to the HJHS. To achieve reliability and validity, it should be applied to pediatric patients aged 4 years and older[15].

FISH

FISH includes seven daily activities (eating, bathing, dressing, sitting in a chair, squatting, walking, and climbing uphill). Each activity is graded on a scale of 1 to 4 based on the degree of independence the patient has in performing the activity. The highest score is 28, in which case the patient can easily perform all activities without assistance. Patients should have no history of bleeding in the last two weeks and should be 7 years of age or older in order to perform the scoring properly[2].

Statistical Analysis

Statistical analyses were performed with SPSS, version 20.0 (SPSS Inc, Chicago, IL, USA). All numerical and categorical data were evaluated using descriptive statistics methods. Numerical continuous parametric variables of the patients were described using mean and standard deviation, and non-parametric numerical continuous variables with median and interquartile range (IQR). Categorical variables were presented as numbers (percentages).

Patients in the study were divided into two groups according to their BMIs as obese/overweight and normal/underweight patients. Student's t test was used to compare the means of parametric numerical data between two independent groups and Mann-Whitney U test to compare the median values of non-parametric numerical data. Chi-square test was applied to analyze categorical data. Results with a p-value <0.05 were considered statistically significant.

RESULTS

A total of 35 male patients with hemophilia A (n=29; 82.9%), and B (n=6; 17.1%) were included in our study. The mean age of the patients was 12.2±4.7 (4-20) years. According to factor levels, 30 patients (85.7%) had severe hemophilia, 4 patients (11.4%) had moderate hemophilia, and 1 patient (2.9%) had mild hemophilia. Table 1 shows the demographic and clinical characteristics of the patients.

Eighty percent (n=28) of the patients were receiving regular prophylaxis. Some patients (n=3; 10.0%) with severe, and moderate hemophilia (n=3: 75.0%), and the only patient with mild hemophilia did not receive prophylaxis. In our study, the mean prophylaxis dose was 20.5±5.3 IU/kg for hemophilia A patients and 25.1±10.8 IU/kg for hemophilia B patients.

The median number of bleeding episodes in the previous year was 1 (IQR: 0-10). No bleeding episodes were observed in 34.3% (n=12) of the patients in the previous year. Target joint development was observed in 14.3% (n=5) of the patients. The number of bleeding

episodes in the previous year was significantly higher in patients with severe hemophilia who did not receive regular prophylactic treatment compared to those who did (median [IQR]: 10 [10-20] vs. 1 [0-6], p=0.049).

FISH was applied to 30 patients, all of whom received a score of 28 points. According to the HJHS, 65.7% (n=23) of the patients were healthy, while 34.3% (n=12) of them had pathological scores. The number of hemorrhagic joints in the previous year was significantly higher in patients with pathological HJHS (HJHS: median [IQR]: 6.5 [0.8-32.5]) compared to those with HJHS within normal range (median [IQR]: 0 [0-3]) (p=0.022), whereas no significant difference was observed in the number of extra-articular hemorrhages between the two groups (median [IQR]: 0 [0-1.5] and 0 [0-0], respectively) (p>0.05). All patients with pathological HJHS (n=12) had severe hemophilia.

Hemophilia patients were obese (n=8: 22.9%) or overweight (n=3: 8.6%). Patients were classified as obese/overweight (n=11: 31.4%) or normal/underweight (n=24: 68.6%). Obese/overweight individuals were significantly younger than those in the other group (p=0.042). When obese/overweight group were compared with the other group, no difference was found in terms of the type of hemophilia, whether the disease was severe or not, the presence of target joints, whether or not they received prophylaxis, and the number of bleeding episodes (p>0.05). It was observed that obese/overweight hemophilia patients received statistically lower doses of prophylaxis per day and per week compared to other patients (p=0.042 and p=0.001). All obese/overweight patients who underwent FISH received a score of 28. There was no difference between being obese/overweight and being normal/underweight in terms of HJHS scoring (p>0.05). Table 2 shows joint health status and clinical differences between BMI groups.

Table 1. Demographic and clinical characteristics of the patients

Characteristics	**n (%)**
Age (years) mean ± sd (min-max)	12.2±4.7 (4-20)
Type of Hemophilia	
Hemophilia A	29 (82.9)
Hemophilia B	6 (17.1)
Clinical classification	
Severe hemophilia	30 (85.7)
Moderate hemophilia	4 (11.4)
Mild hemophilia	1 (2.9)
Classification by BMI	
Underweight	4 (11.4)
Normal	20 (57.1)
Overweight	3 (8.6)
Obese	8 (22.9)

BMI: Body mass index, sd: Standard deviation, min-max: Minimum-maximum

DISCUSSION

In recent years, advancements in the management of hemophilia-such as improved access to factor concentrates, personalized prophylaxis strategies, long-acting factor preparations, and a multidisciplinary treatment approach-have significantly extended life expectancy of the patients, bringing it on par with that of the general population. However, one emerging morbidity that poses a challenge, particularly in the context of preserving joint health, is obesity. In light of this information, we conducted an evaluation of the clinical characteristics of patients with hemophilia and explored the association between obesity and disease outcomes.

In our study, hemophilia patients were obese (22.9%) or obese/overweight. These incidence rates were significantly higher than the general population, where 8.2% of children aged 6-18 years are obese, and 22.5% are obese/overweight, according to the Turkey Nutrition and Health Survey 2010 report[16]. Additionally, a meta-analysis of 76 studies in Turkey found that the prevalence of obesity among male individuals aged 5-19 years was 7.4%[17]. These findings suggest that the rate of obesity in our hemophilia patients is notably higher than in the general Turkish population. In a 2019 study of 254 hemophilia patients with a median age of 13 years in Germany, the obesity/overweight rate was reported at 25.2%[8]. A similar rate of 25.6% was observed in a study conducted in Taiwan among hemophilia patients under 18 years of age[6]. Additionally, a 2018 meta-analysis of 28 studies from Europe and North America found an obesity/overweight rate of 31%, which aligns closely with our study findings[1].

In addition to the challenges posed by obesity in hemophilia patients, effective management of the disease remains crucial, particularly through primary prophylaxis. While a definitive cure for hemophilia remains elusive, primary prophylaxis stands as the cornerstone of treatment, aiming to maintain hemostasis and prevent bleeding episodes[18]. Hemophilia prophylaxis regimens in children vary globally, with high-dose regimens (25-40 IU/kg for hemophilia A, 40-60 IU/kg for hemophilia B), medium-dose regimens (15-

Table 2. Comparison of BMI groups in terms of clinical features and joint health status

		Obese/overweight n: 11 (31.4%)	Normal/underweight n: 24 (68.6%)	p-value
Age (years) mean ± sd (min-max)		9.8±4.7 (5-18)	13.3±4.4 (4-20)	0.042
Type of hemophilia n (%)	A B	11 (38.0) 0 (0.0)	18 (62.0) 6 (100.0)	0.083
Clinical classification of hemophilia n (%)	Severe Moderate/mild	9 (30.0) 2 (40.0)	21 (70.0) 3 (60.0)	0.509
Prophylaxis n (%)	Yes No	8 (28.6) 3 (42.9)	20 (71.4) 4 (57.1)	0.381
Prophylaxis dose (IU/kg) daily mean ± sd (min-max)		17.3±3.5 (12.9-23.8)	23.1±7.2 (12.1-39.2)	0.042
Prophylaxis dose (IU/kg) weekly mean ± sd (min-max)		35.8±9.9 (23.8-53.9)	57.5±21.3 (20.0-97.4)	0.001
Number of bleedings in the last year median (IQR)		2 (0-10)	1 (0-9)	0.856
Target joint n (%)	Yes No	2 (40.0) 9 (30.0)	3 (60.0) 21 (70.0)	0.509
FISH n (%)	Healthy Patologic	8 (26.7) 0 (0.0)	22 (73.3) 0 (0.0)	
HJHS n (%)	Healthy Patologic	7 (30.4) 4 (33.3)	16 (69.6) 8 (66.7)	0.329

BMI: Body mass index, FISH: Functional Independence Score in Hemophilia, HJHS: Hemophilia Joint Health Score, IQR: Interquartile range, sd: Standard deviation, min-max: Minimum-maximum

25 IU/kg for hemophilia A, 20-40 IU/kg for hemophilia B), and low-dose regimens (10-15 IU/kg for both types) [19]. High- and medium-dose regimens initiated early in life have been shown to reduce annual bleeding rates by 90% while significantly preventing development of joint damage and degenerative disease[20,21]. In our study, the mean prophylactic dose was 20.5±5.3 IU/kg for hemophilia A and 25.1±10.8 IU/kg for hemophilia B, indicating that both groups received doses within the recommended ranges.

Today, the goal of treatment for hemophilia patients is to have no bleeding episodes at all[22,23]. Prophylactic treatment has been shown to be superior to on-demand treatment in preventing joint damage in hemophilia patients[20]. In our study, 34.3% (n=12) of patients with hemophilia, all of whom were receiving prophylaxis, had no bleeding episode within the previous year. Indeed, over the years, the number of target joints has declined, which can be attributed to the widespread use of prophylactic factor therapy. In our study, 14.3% (n=5) of patients with hemophilia developed a target joint. In a study conducted in our clinic in 2011 with 38 hemophilia patients, target joints were present in 39.5% (n=15) of the patients[24].

In this study, no significant differences were observed between the obese/overweight and the normal/underweight groups in terms of target joint involvement or bleeding frequency. Interestingly, despite receiving lower factor doses (IU/kg), the obese/overweight group achieved treatment outcomes, comparable to those with normal/underweight groups highlighting a noteworthy aspect of treatment efficacy in this population. This could be due to differences in how clotting factors are distributed and metabolized in the body. Various pharmacokinetic studies have indicated that overweight patients consume less FVIII per kilogram due to having a lower plasma volume in adipose tissue, and they are given more factor than they actually need[8]. Seaman et al.[25] suggested that patients with hemophilia may benefit from an individualized pharmacokinetic analysis using lean body mass and ideal body weight to determine the most accurate and potentially cost-effective method for achieving targeted FVIII recovery. On the other hand, another reason for the comparable outcome could be that overweight individuals may engage in less physically demanding activities, thereby reducing their risk of bleeding[26]. Obese/overweight hemophilia patients in our study were significantly younger than

normal/underweight patients (p=0.042), likely due to movement restrictions imposed by protective parental behaviors. Parents often limit their children's physical activities due to bleeding risks, which also reduces social interactions[27]. Such overprotective behaviors are common in families with chronically ill children, particularly in cultures where mothers are the primary caregivers[28]. In line with this, Kantarcıoğlu et al.[29] found that mothers of children with hemophilia were more protective than those of children with leukemia. The protective behaviors of parents of younger hemophilia patients may have reduced their physical activity, which, along with fewer bleeding episodes, could have contributed to their overweight status.

Monitoring joints with HJHS, a validated and reliable tool for assessing treatment effectiveness in patients with hemophilia, is crucial[14,30,31]. In our study, 34.3% (n=12) of patients had pathological joints according to HJHS, and all were diagnosed with severe hemophilia. These patients had a statistically higher number of bleedings in the previous year (p=0.008), confirming the strong correlation between recurrent bleeding episodes and joint damage. The patients with pathological joints were obese/overweight (n=4), and normal/underweight (n=8) according to HJHS which may also be related to the fact that obese/overweight patients are younger, with less time elapsed for joint damage, thanks to the protective behaviors of their parents.

Recurrent joint hemorrhages in patients with hemophilia may lead to musculoskeletal system changes, resulting in impaired functional capacity. FISH scoring developed for patients with hemophilia measures joint functions with daily activity parameters[32]. In our study, all 30 hemophilia patients whose ages were suitable for FISH scoring received 28 points, indicating that their joint functions were independent during daily activities. In a study reported by Liu et al.[33] from China in 2020, even low-dose prophylaxis (10-15 IU/kg, 2-3 days per week) was shown to improve FISH and other joint scores in hemophilia patients aged 4-18 years compared to on-demand treatment. In the same study, FISH scores of patients receiving low-dose prophylaxis ranged between 24-26 points. However, these patients received tertiary prophylaxis. In a study reported from India in 2020, FISH scores of the patients ranged between 13-28 points[34]. It can be said that our patients were able to maintain independence in their daily activities as also revealed by their FISH scores thanks to receiving prophylaxis at an effective dose before the development of joint damage. The contribution of the treatments to recovery is measured by repeating the FISH scoring at certain periods[33,35]. In a 2015 study conducted at our clinic with a similar patient group, FISH scores ranged from 22 to 28 points. Remarkably, all of our patients, irrespective of their obesity status, currently scored 28 points, underscoring the significant role of effective treatment in promoting recovery[36].

Study Limitations

The fact that the ROM of the patients was not measured in our study and that there was no scoring that measured the activities of the patients limited generalisability of our study findings. Additionally, as it is a single-center study, support from studies conducted at other centers is needed to validate our findings.

CONCLUSION

In conclusion, parameters such as annual counts of bleeding episodes, target joint formation, HJHS, and FISH help assess whether prophylaxis has been administered at an effective dose before development of joint damage. Our patients received prophylaxis within the recommended dose range, but obese/overweight patients had statistically lower weekly doses compared to normal/underweight patients. Despite this, there was no difference in annual counts of bleeding episodes or target joint formation between the groups. Furthermore, while HJHS results were similar, all obese/overweight patients were fully independent in their daily activities according to FISH. Our findings suggest that obese/overweight patients can receive adequate treatment with lower doses. However, personalized dosing would be the ideal approach. We believe that pharmacokinetic studies based on ideal or lean body weight could help determine the optimal dose for each patient, improving treatment accuracy.

Ethics

Ethics Committee Approval: Approval of the Local Research Ethics Committee of University of Health Sciences Turkey, Dr. Behçet Uz Pediatric Diseases and Surgery Training and Research Hospital (approval number: 2021/03-09, dated: 11.02.2021)

Informed Consent: Written informed consent were obtained from the parents of the patients.

Footnotes

Author Contributions

Concept: H.Ö., Y.O., Design: H.Ö., Y.O., Data Collection or Processing: H.Ö., D.Ç., Analysis or Interpretation: H.Ö., D.Ç., Literature Search: H.Ö., Y.O., Writing: H.Ö., Y.O., D.Ç.

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REFERENCES

1. Wilding J, Zourikian N, Di Minno M, Khair K, Marquardt N, Benson G, et al. Obesity in the global haemophilia population: prevalence, implications and expert opinions for weight management. Obes Rev. 2018;19(11):1569-84. doi: 10.1111/obr.12746
2. Poonnoose PM, Thomas R, Keshava SN, Cherian RS, Padankatti S, Pazani D, et al. Psychometric analysis of the Functional Independence Score in Haemophilia (FISH). Haemophilia. 2007;13(5):620-6. doi: 10.1111/j.1365-2516.2007.01508.x
3. Manco-Johnson MJ, Soucie JM, Gill JC; Joint Outcomes Committee of the Universal Data Collection, US Hemophilia Treatment Center Network. Prophylaxis usage, bleeding rates, and joint outcomes of hemophilia, 1999 to 2010: a surveillance project. Blood. 2017;129(17):2368-74. doi: 10.1182/blood-2016-02-683169
4. Nilsson IM, Berntorp E, Löfqvist T, Pettersson H. Twenty-five years' experience of prophylactic treatment in severe haemophilia a and b. J Intern Med. 1992;232(1):25-32. doi: 10.1111/j.1365-2796.1992.tb00546.x
5. Wong TE, Majumdar S, Adams E, Bergman S, Damiano ML, Deutsche J, et al. Overweight and obesity in hemophilia: a systematic review of the literature. Am J Prev Med. 2011;41(6 Suppl 4):S369-75. doi: 10.1016/j.amepre.2011.09.008
6. Chang CY, Li TY, Cheng SN, Pan RY, Cheng CN, Wang HJ, et al. Obesity and overweight in patients with hemophilia: prevalence by age, clinical correlates, and impact on joint bleeding. J Chin Med Assoc. 2019;82(4):289-294. doi: 10.1097/JCMA.0000000000000047
7. Hofstede FG, Fijnvandraat K, Plug I, Kamphuisen PW, Rosendaal FR, Peters M. Obesity: a new disaster for haemophilic patients? A nationwide survey. Haemophilia. 2008;14(5):1035-8. doi: 10.1111/j.1365-2516.2008.01806.x
8. Olivieri M, Königs C, Heller C, Horneff S, Oldenburg J, Halimeh S, et al. Prevalence of obesity in young patients with severe haemophilia and ıts potential ımpact on factor VIII consumption in Germany. Hamostaseologie. 2019;39(4):355-9. doi: 10.1055/s-0039-1677874
9. Soucie JM, Wang C, Siddiqi A, Kulkarni R, Recht M, Konkle BA, et al. The longitudinal effect of body adiposity on joint mobility in young males with haemophilia a. Haemophilia. 2011;17(2):196-203. doi: 10.1111/j.1365-2516.2010.02400.x
10. Soucie JM, Cianfrini C, Janco RL, Kulkarni R, Hambleton J, Evatt B, et al. oint range-of-motion limitations among young males with hemophilia: prevalence and risk factors. Blood. 2004;103(7):2467-73. doi: 10.1182/blood-2003-05-1457
11. Biere-Rafi S, Haak BW, Peters M, Gerdes VE, Büller HR, Kamphuisen PW. The impairment in daily life of obese haemophiliacs. Haemophilia. 2011;17(2):204-8. doi: 10.1111/j.1365-2516.2010.02417.x
12. Kahan S, Cuker A, Kushner RF, Maahs J, Recht M, Wadden T, et al. Prevalence and impact of obesity in people with haemophilia: review of literature and expert discussion around implementing weight management guidelines. Haemophilia. 2017;23(6):812-20. doi: 10.1111/hae.13291
13. Neyzi O, Bundak R, Gökçay G, Günöz H, Furman A, Darendeliler F, et al. Refer Reference values for weight, height, head circumference, and body mass ındex in Turkish children. J Clin Res Pediatr Endocrinol. 2015;7(4):280-93. doi: 10.4274/jcrpe.2183
14. Sun J, Hilliard PE, Feldman BM, Zourikian N, Chen L, Blanchette VS, et al. Chinese hemophilia joint health score 2.1 reliability study. Haemophilia. 2014;20(3):435-40. doi: 10.1111/hae.12330
15. Hilliard P, Funk S, Zourikian N, Bergstrom BM, Bradley CS, McLimont M, et al. Hemophilia joint health score reliability study. Haemophilia. 2006;12(5):518-25. doi: 10.1111/j.1365-2516.2006.01312.x
16. T.C. Sağlık Bakanlığı. Türkiye beslenme ve sağlık araştırması 2010: beslenme durumu ve alışkanlıklarının değerlendirilmesi sonuç raporu. T.C. Sağlık Bakanlığı Yayın No:931, 2014. http://www.sagem.gov.tr/TBSA_Beslenme_Yayini.pdf Accessed 15.04.2021.
17. Alper Z, Ercan İ, Uncu Y. A meta-analysis and an evaluation of trends in obesity prevalence among children and adolescents in Turkey: 1990 through 2015. J Clin Res Pediatr Endocrinol. 2018;10(1):59-67. doi: 10.4274/jcrpe.5043
18. Berntorp E, Boulyjenkov V, Brettler D, Chandy M, Jones P, Lee C, et al. Modern treatment of haemophilia. Bull World Health Organ. 1995;73(5):691-701. https://pubmed.ncbi.nlm.nih.gov/8846496/
19. Srivastava A, Santagostino E, Dougall A, Kitchen S, Sutherland M, Pipe SW, et al. WFH guidelines for the management of hemophilia, 3rd edition. Haemophilia. 2020;26 Suppl 6:1-158. doi: 10.1111/hae.14046. Epub 2020. Erratum in: Haemophilia. 2021;27(4):699. doi: 10.1111/hae.14308
20. Manco-Johnson MJ, Abshire TC, Shapiro AD, Riske B, Hacker MR, Kilcoyne R, et al. Prophylaxis versus episodic treatment to prevent joint disease in boys with severe hemophilia. N Engl J Med. 2007;357(6):535-44. doi: 10.1056/NEJMoa067659
21. Fischer K, Steen Carlsson K, Petrini P, Holmström M, Ljung R, van den Berg HM, et al. Intermediate-dose versus high-dose prophylaxis for severe hemophilia: comparing outcome and costs since the 1970s. Blood. 2013;122(7):1129-36. doi: 10.1182/blood-2012-12-470898
22. Reding MT, Pabinger I, Holme PA, Poulsen L, Negrier C, Chalasani P, et al. Confirmed long-term safety and efficacy of prophylactic treatment with BAY 94-9027 in severe haemophilia a: final results of the PROTECT VIII extension study. Haemophilia. 2021;27(3):e347-e356. doi: 10.1111/hae.14297
23. Kihlberg K, Baghaei F, Bruzelius M, Funding E, Andre Holme P, Lassila R, et al. Treatment outcomes in persons with severe haemophilia b in the Nordic region: The B-NORD study. Haemophilia. 2021;27(3):366-374. doi: 10.1111/hae.14299
24. Oymak Y. hemofilili hastalarda eklem skorlarının artropatiyi tanımlamadaki rolü ve eklem bulgularının yaşam kalitesine etkisi. (Tez). İzmir: Dr. Behçet Uz Çocuk Hastalıkları ve Cerrahisi Eğitim ve Araştırma Hastanesi;2011.
25. Seaman CD, Yabes JG, Lalama CM, Ragni MV. Factor VIII concentrate dosing with lean body mass, ideal body weight and total body weight in overweight and obesity: a randomized, controlled, open-label, 3 × 3 crossover trial. Haemophilia. 2021;27(3):351-357. doi: 10.1111/hae.14285
26. Cooper AR, Page A, Fox KR, Misson J. Physical activity patterns in normal, overweight and obese individuals using minute-by-minute accelerometry. Eur J Clin Nutr. 2000;54(12):887-94. doi: 10.1038/sj.ejcn.1601116
27. Wittmeier K, Mulder K. Enhancing lifestyle for individuals with haemophilia through physical activity and exercise: the role of physiotherapy. Haemophilia. 2007;13 Suppl 2:31-7. doi: 10.1111/j.1365-2516.2007.01504.x

28. Evim MS, Kantarcıoğlu AÇ. Problem behaviours and over protective maternal attitudes in hemophilia. J Curr Pediatr. 2020;18(1):74-84. https://dergipark.org.tr/tr/download/article-file/1053620

29. Kantarcıoğlu AÇ, Evim MS. Assessment of Overprotective Parenting Attitudes and Emotional Status among Mothers in Pediatric Thalassemia, Hemofilia and Leukemia Patients in Bursa. J Curr Pediatr. 2018;16:(3):37-50. Available from: https://dergipark.org.tr/tr/pub/pediatri/issue/40492/485250.

30. Feldman BM, Funk SM, Bergstrom BM, Zourikian N, Hilliard P, van der Net J, et al. Validation of a new pediatric joint scoring system from the International hemophilia prophylaxis study group: validity of the hemophilia joint health score. Arthritis Care Res (Hoboken). 2011;63(2):223-30. doi: 10.1002/acr.20353

31. Bladen M, Main E, Hubert N, Koutoumanou E, Liesner R, Khair K. Factors affecting the haemophilia joint health score in children with severe haemophilia. Haemophilia. 2013;19(4):626-31. doi: 10.1111/hae.12108

32. Poonnoose PM, Manigandan C, Thomas R, Shyamkumar NK, Kavitha ML, Bhattacharji S, et al. Functional Independence Score in Haemophilia: a new performance-based instrument to measure disability. Haemophilia. 2005 Nov;11(6):598-602. doi: 10.1111/j.1365-2516.2005.01142.x

33. Liu Y, Chen L, Li K, Shi M, Poon MC. Severe haemophilia a children on low-dose tertiary prophylaxis showed less joint deterioration and better maintenance of functional independence than children on on-demand treatment: a 6-year follow-up study. Haemophilia. 2020;26(5):779-785. doi: 10.1111/hae.14016

34. Guha A, Rai A, Nandy A, Mondal T, Pandit N, Guha S, et al. Joint scores in hemophilic arthropathy in children: developing country perspectives. Eur J Rheumatol. 2019 Dec 16;7(1):26-30. doi: 10.5152/eurjrheum.2019.19040

35. Tat NM, Can F, Sasmaz HI, Tat AM, Antmen AB. The effects of manual therapy on musculoskeletal system, functional level, joint health and kinesiophobia in young adults with severe haemophilia: a randomized pilot study. Haemophilia. 2021;27(2):e230-e238. doi: 10.1111/hae.14031

36. Oymak Y, Yildirim AT, Yaman Y, Gurcinar M, Firat A, Cubuckcu D, et al. The effectiveness of tools for monitoring hemophilic arthropathy. J Pediatr Hematol Oncol. 2015;37(2):e80-5. doi: 10.1097/MPH.0000000000000210