Prevalence of Modifiable Cardiovascular Risk Factors Associated With Lifestyle Habits in Adults With Hemophilia in Croatia

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SUMMARY

The aim of this study was to determine the prevalence of habits and lifestyle factors associated with increased cardiovascular risk in patients with hemophilia, including smoking, alcohol consumption, and physical activity, as well as the prevalence of anthropometric measures, such as body mass index (BMI) and waist circumference, in the same population.

The study included a total of 96 adult patients with hemophilia A or B. All patients were treated at the Reference Center for Inherited and Acquired Disorders of Hemostasis in Croatia at University Hospital Centre Zagreb.

Statistical analysis included appropriate numerical features of descriptive statistics, as well as suitable statistical models. Categorical variables were described using absolute and relative frequencies, while numerical variables were presented depending on their distribution type.

Regarding lifestyle factors, 39.6% of the patients were active smokers and 75.0% reported consuming alcohol. Almost all patients (97.9%) met the minimum for physical activity the Croatian Institute of Public Health. However, 38.5% did not engage in intense physical activity. The largest proportion of participants were overweight, with a BMI of 25–29.9 kg/m^2 (41.7%). Overall, 67.7% of the patients were classified as either overweight or obese, representing approximately two-thirds of the study population. These findings indicate that Croatian patients with hemophilia demonstrate higher rates of smoking, alcohol consumption, and overweight/obesity compared not only with hemophilia populations reported in previous studies from other countries, but also with the general population in Croatia, highlighting the importance of taking action to reduce cardiovascular risk in this patient group.

KEYWORDS

Hemophilia; BMI; Smoking; Alcohol; Physical activity

Introduction

Hemophilia is classified as a rare disease according to the World Health Organization (WHO), and it comes in two forms: hemophilia A and B[1]. With modern hemophilia treatments, patient life expectancy has increased so much that, according to some studies, it is now similar to the general population[2]. As in the general population, aging in patients with hemophilia is associated with the development of age-related conditions, including an increase in cardiovascular risk factors that may contribute to cardiovascular disease. Treatment of cardiovascular disease in this population is especially challenging due to the need to balance the risk of bleeding against ischemic events[3,4].

Lifestyle factors further contribute to cardiovascular risk. Smoking is a strong independent risk factor, responsible for approximately 17.9% of all cardiovascular deaths, while excessive alcohol consumption, particularly in high amounts or binge patterns, is associated with hypertension, coronary artery disease, stroke, arrhythmias, and heart failure, through mechanisms including elevated blood pressure, vascular inflammation, and metabolic dysregulation[5,6]. Overweight and obesity are also independent risk factors, with body mass index (BMI) as the most common measure to classify participants as overweight or obese. These conditions are influenced by factors such as diet, socio-demographic characteristics, and physical activity[7].

Therefore, this study aimed to examine the prevalence of lifestyle habits that may contribute to elevated cardiovascular risk among adults with hemophilia in Croatia.

Patients and methods

The study included a total of 96 adult patients with hemophilia A or hemophilia B. All patients were treated at the Center for Hemophilia in the Department of Hematology, Internal Medicine Clinic at University Hospital Centre (UHC) Zagreb, and the Reference Center for Inherited and Acquired Disorders of Hemostasis in Croatia. The study was approved by the ethics committees of UHC Zagreb and the School of Medicine, University of Zagreb.

The study was conducted in full compliance with the General Data Protection Regulation, with strict safeguards in place to ensure data confidentiality and participant anonymity. The diagnosis of hemophilia was established based on factor VIII or IX activity, according to established guidelines[8].

For each patient, functions and habits were examined, with particular emphasis on smoking, alcohol consumption, and the level of physical activity, due to their importance in assessing cardiovascular risk. Anthropometric measurements, including body height and body weight were obtained for all participants. Body height was measured in the standing position without footwear, while body weight was assessed without heavy clothing using a calibrated medical scale.

The body mass index (BMI) was calculated as body weight in kilograms divided by the square of height in meters:

$$\text{BMI} = \frac{\text{body weight (kg)}}{\text{height}^2\ (\text{m}^2)}$$

According to WHO criteria, BMI values from 18.5 to 24.9 kg/m² are considered normal. A BMI below 18.5 kg/m² indicates underweight, whereas a BMI between 25 and 29.9 kg/m² is classified as overweight. Obesity is defined as a BMI of 30 kg/m² or higher and is further categorized into three classes. Class I obesity is defined as a BMI of 30–34 kg/m², Class II as a BMI of 35–39.9 kg/m², and Class III as a BMI ≥ 40 kg/m², which is considered severe/extreme obesity[9].

Waist circumference was measured with patients standing upright and the abdomen relaxed, immediately after a normal exhalation. Measurements were taken at the level of the umbilicus, midway between the lower ribs and the iliac crest, following standard anthropometric procedures.

According to WHO guidelines, men with a waist circumference exceeding 94 cm were classified as being at increased risk, whereas those with a waist circumference greater than 102 cm were considered at very high risk for the development of metabolic syndrome, type 2 diabetes, hypertension, and cardiovascular disease[10].

Data analysis

All collected data were systematically recorded and managed in a Microsoft Excel–based database. Statistical analysis included appropriate numerical features of descriptive statistics, as well as suitable statistical models, and was performed using the R software (RStudio version 0.99.903).

Categorical variables were described using absolute and relative frequencies, while numerical variables were presented depending on their distribution. Normally distributed numerical variables were expressed as mean ± standard deviation (SD), whereas non-normally distributed variables were summarized using the median and interquartile range (IQR).

Results

Of the 96 adult patients with hemophilia included in this study, the majority had hemophilia A (87.5%), while a smaller proportion had hemophilia B (11.5%). The median age of all patients was 49 (IQR 36.00–58.25) years. The largest proportion of all participants was in the 30–39 years age group (42.7%), followed by the 40–49 years age group (26.0%), the 60–69 years age group (12.5%), patients older than 70 years (10.4%), and finally patients aged 18–29 years (8.3%), as illustrated in Table 1.

Table 1. Characteristics of patients with hemophilia

Patients' characteristics		Hemophilia (total) N = 96
Age		Median (IQR) 49 (36.00–58.25)
		Mean (SD)
Waist circumference		98.53 (13.61)
BMI		27.06 (4.70)
BMI classification	Malnutrition / < 18.5 kg/m^2	4 (4.2)
	Normal body weight / 18.5–24.9 kg/m^2	27 (28.1)
	Overweight / 25–29.9 kg/m^2	40 (41.7)
	Obesity / > 30 kg/m^2	25 (26.0)

SD = standard deviation; IQR = interquartile range

Waist circumference was measured for all patients, with a mean value of 98.53 cm (SD 13.61) and the calculated mean BMI was 27.06 kg/m^2 (SD 4.70), as shown in Table 1. Among the patients, those classified as overweight (BMI 25–29.9 kg/m^2) were the largest group (41.7%), followed by patients with normal weight (BMI 18.5–24.9 kg/m^2) at 28.1%. Patients with obesity (BMI ≥ 30 kg/m^2) accounted for 26.0%, while underweight patients (BMI < 18.5 kg/m^2) were the smallest group at 4.2%, as shown in Table 1. The overall proportion of patients with BMI classifications of overweight and obesity was 67.7%, or approximately 2/3 of all patients.

The prevalence of habits and lifestyle factors associated with increased cardiovascular risk in patients with hemophilia, including smoking, alcohol consumption, and physical activity, varied. Among all participants, 60.4% were non-smokers. Of the 39.6% who were active smokers, the majority consumed up to half a pack of cigarettes daily (39.47%), followed by those who smoked between half a pack and a full pack daily (28.95%). Their smoking habits are detailed in Table 2.

Table 2. Cigarette consumption in all participants

Smoking	**N (%)**	
Yes	38 (39.6)	
Cigarette consumption	All participants	Smokers
non-smokers	58 (60.4)	0 (0)
up to half a pack per day	15 (15.6)	15 (39.47)
up to one pack per day	11 (11.5)	11 (28.95)
more than 1 pack per day	5 (5.2)	5 (13.16)
ex-smokers > 12 months	7 (7.3)	7 (18.42)

Table 3. Alcohol consumption in all participants

Alcohol	N (%)	
Yes	72 (75.0)	
Alcohol consumption	All participants	Participants reporting alcohol consumption
None	24 (25.0)	0 (0)
Daily consumption: < 5 drinks	1 (1.0)	1 (1.39)
Weekly consumption: < 5 drinks	17 (17.7)	17 (23.6)
Weekly consumption: 5–10 drinks	15 (15.6)	15 (20.8)
Monthly consumption: < 5 drinks	32 (33.3)	32 (44.5)
Monthly consumption: 5–10 drinks	7 (7.3)	7 (9.7)

The majority of the patients, as many as 75.0%, consumed alcohol, ranging from occasional to regular consumption. The frequency of alcohol consumption is divided based on daily, weekly, and monthly consumption in Table 3. The most common pattern of alcohol consumption was on a monthly basis, with fewer than 5 glasses of alcoholic beverages per month (44.5%).

According to the CIPH guidelines of the Croatian Institute of Public Health (CIPH), the recommendation for physical activity is 150–300 minutes of moderate activity or 30 minutes of brisk walking < 5 times a week. Nearly all patients (97.9%) met these criteria, with the majority engaging in moderately intense physical activity through daily activities more than five times a week (81.2%). While 38.5% of the patients did not engage in intense physical activity, more than 39.6% met the recommended levels of at least 75–150 minutes per week, or more than 3–5 sessions of 20–30 minutes per week, as detailed in Table 4.

Table 4. Physical activity in all participants

Physical activity	N (%)
Yes	94 (97.9)
Moderate physical activity	
No moderate physical activity	2 (2.1)
< 150–300 minutes of moderate activity	14 (14.6)
150–300 minutes of moderate activity	2 (2.1)
> 150–300 minutes of moderate activity	78 (81.2)
Intense physical activity	
No intense physical activity	37 (38.5)
< 75–150 minutes per week	16 (16.7)
75–150 minutes per week	5 (5.2)
> 75–150 minutes per week	38 (39.6)

Discussion

The results of this study showed that the majority of our patients had hemophilia A, which corresponds to the higher prevalence of hemophilia A in previous studies[11].

Practically a quarter of the patients (39.6%) were active smokers, which is slightly higher than the average of the general Croatian population (37%), according to the latest study by CIPH and the Ivo Pilar Institute of Social Sciences from 2023[12]. Data from prior studies involving only patients with hemophilia indicate a smoking prevalence of 39%[7]; slightly lower than in this study.

This leads to the conclusion that the prevalence of active smokers among Croatian patients with hemophilia is higher than in the general population of Croatia, as well as than what is reported in hemophilia populations in other countries.

Previous studies have reported that 45.2% of patients with hemophilia consume alcohol[7]. In contrast, our findings indicate that as many as 75% of such patients reported alcohol consumption, ranging from occasional to regular use. These results suggest that alcohol consumption among Croatian patients with hemophilia is considerably higher than reported in hemophilia populations from other countries. The most common pattern of alcohol consumption among the patients in this study was on a monthly basis (54.2%), and 44.5% of patients from this group consumed less than 5 alcoholic drinks per month, while 9.7% consumed 5–10 alcoholic drinks per month. According to a CIPH study published in 2021, based on the European Union legal framework, the third cycle of the European Health Interview Survey found that just over 26.5% of the male population consumes alcohol on a monthly basis, which is significantly lower than the 54.2% of participants with hemophilia A and B in this study who consumed alcohol monthly[13].

Considering that alcohol consumption is a modifiable cardiovascular risk factor and given its notably higher prevalence among Croatian patients

with hemophilia compared with both the general Croatian population and hemophilia cohorts from other countries, the importance of reducing alcohol consumption in this population arises as a highly important preventive measure. Addressing this modifiable behavior should therefore represent a priority in strategies aimed at reducing cardiovascular risk in this population.

As many as 97.9% of the patients of this study met the CIPH recommendation for minimum physical activity per week, which is 150–300 minutes of moderate activity, or 30 minutes of moderate physical activity < 5× a week[14]. This criterion was predominantly fulfilled through activities of daily living. However, 38.5% of the patients reported they do not engage in more intense physical activity. According to previous studies, 58.1% of individuals with hemophilia engage in regular physical activity. However, details regarding the duration of such activity were not provided, preventing an objective comparison[15]. Data from the European Health Interview Survey indicate that only 19.5% of the general population achieves the recommended minimum of at least 150 minutes of aerobic physical activity per week, whereas an even lower proportion (15.7%) reports engaging in muscle-strengthening activities at least twice a week[14].

Given the substantial gap between the European Health Interview Survey and our results, it is likely that patients' responses were not obtained through a standardized or fully objective method. Nevertheless, in the absence of more precise comparative data, the present study indicated that patients with hemophilia achieve the recommended minimum levels of physical activity, primarily through routine daily activities rather than structured exercise or intentional training.

In this study, the average BMI of all patients with hemophilia A and B was 27.06 kg/m², placing the average BMI of all patients within the range of 25–29.9 kg/m², which is classified as overweight[9]. Considering the distribution of all patients, 67.7% of all patients with hemophilia in this study fell into the categories of overweight and obesity, comprising approximately two-thirds of the patients in this study. Previous studies have shown a significant proportion of patients with hemophilia falling into the overweight and obesity categories, but it is important to note that the proportion of overweight and obese patients in this study is higher than what was observed in previous research[16,17]. According to a meta-analysis of epidemiological data on overweight and obesity over a 15-year period (2003–2018) in patients with hemophilia, the combined prevalence of overweight and obesity among individuals with hemophilia in Europe and North America was estimated to be 31%, which is significantly lower than the 67.7% in this study[17]. This finding directly points to an increased need for weight reduction interventions in the patients from this study.

In comparison, the overall prevalence of overweight, obesity, and increased waist circumference in the general population of Croatia is 38.11%, 20.34%, and 43.52%, respectively[18]. This indicates that 58.45% of the general population in Croatia is categorized as overweight or obese. Although this figure is high even for the general population, our results demonstrated that patients with hemophilia exhibit a greater prevalence of overweight and obesity (67.7%) than both previous studies in other hemophilia cohorts and the general population in Croatia.

The average waist circumference among the patients was 98.53 cm, with an SD of 13.61 cm. Waist circumference exceeding 94 cm in men is recognized as a risk factor for the development of metabolic syndrome, type 2 diabetes, hypertension, and cardiovascular disease, according to WHO guidelines[10]. These findings suggest that patients with hemophilia in this study are at a substantially increased risk for developing the previously mentioned conditions, highlighting the need for targeted preventive and monitoring strategies in this population.

Conclusion

This study revealed a high cardiovascular risk among Croatian patients with hemophilia, with 39.6% being active smokers, 75.0% consuming alcohol, and 97.9% engaging in minimal recommended physical activity. Combined with a mean waist circumference of 98.53 cm (SD 13.61) and a mean BMI of 27.06 kg/m² (SD 4.70) — resulting in 67.7% of the participants being classified as overweight or obese — these findings indicate that Croatian patients with hemophilia exhibit higher rates of smoking, alcohol consumption, and overweight/obesity compared not only with hemophilia populations reported in previous studies from other countries, but also with the general population in Croatia, highlighting the importance of taking action to reduce cardiovascular risk in these patients.

INFORMED CONSENT Informed patient consent was obtained from all individual participants in the study.

CONFLICT OF INTEREST The authors declare no conflict of interest. ■

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SAŽETAK

Prevalencija modificirajućih čimbenika kardiovaskularnog rizika povezanih sa životnim navikama kod odraslih osoba s hemofilijom u Hrvatskoj

Petra Bubalo i Silva Zupančić-Šalek

Svrha ovog istraživanja bila je utvrditi prevalenciju navika i životnih čimbenika povezanih s povećanim kardiovaskularnim rizikom kod bolesnika s hemofilijom, uključujući pušenje, konzumaciju alkohola i tjelesnu aktivnost, kao i prevalenciju antropometrijskih pokazatelja kao što su indeks tjelesne mase (BMI) i opseg struka u istoj skupini pacijenata.

U istraživanje je uključeno ukupno 96 odraslih bolesnika s hemofilijom A/B. Svi su bolesnici liječeni u Referentnom centru za nasljedne i stečene bolesti hemostaze u Hrvatskoj u Kliničkom bolničkom centru Zagreb.

Statistička analiza podataka uključivala je prikladna numerička i grafička obilježja deskriptivne statistike te odgovarajuće statističke modele. Kategorijske varijable deskriptivno su prikazane pomoću apsolutnih i relativnih frekvencija, a numeričke varijable ovisno o distribuciji.

Među svim ispitanicima, 39,6 % bili su aktivni pušači. Većina sudionika, čak 75,0 %, konzumirala je alkohol. Minimalnu tjelesnu aktivnost propisanu od strane Hrvatskog zavoda za javno zdravstvo ispunjavalo je 97,9 % ispitanika, dok je 38,5 % prijavilo da se ne bavi nikakvom intenzivnijom tjelesnom aktivnošću. Najveći udio ispitanika bio je prekomjerne tjelesne težine s BMI-jem između 25 i 29,9 kg/m^2 (41,7 %). Prekomjerna tjelesna težina i pretilost zabilježene su u 67,7 % ispitanika, što čini približno dvije trećine svih ispitanika. Ovi rezultati upućuju na to da oboljeli od hemofilije u Hrvatskoj pokazuju veće stope pušenja, konzumacije alkohola te prekomjerne tjelesne mase i pretilosti u usporedbi ne samo s oboljelima od hemofilije u drugim zemljama, već i s općom populacijom Hrvatske. To naglašava potrebu za ciljanom intervencijom usmjerenom na smanjenje kardiovaskularnog rizika u ovoj populaciji.

KLJUČNE RIJEČI

Hemofilija; BMI; Pušenje; Alkohol; Tjelesna aktivnost