

Lipid Profile of Children and Adolescents with Hemophilia at Zagazig University Hospitals

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ABSTRACT

Background: The increased management of hemophilia has led to an increase in age-related problems in this population. These patients have high rates of cardiovascular risk factors, such as high blood pressure, hypercholesterolemia, and diabetes, which may have an impact on their overall health and healthcare costs.

Objectives: To investigate hemophilia patients for lipid profile changes and its clinical impacts.

Subjects and methods: this case-control study was conducted in Hematology Unit and Outpatients' Hematology Clinic of Pediatric Department at Zagazig University Hospitals over 6-month period. This study was conducted on 153 subject divided into 87 patients with clinical and laboratory diagnosis of hemophilia (65 hemophilia A and 22 hemophilia B) and 66 age and sex matched healthy children as a control group. All the studied groups were subjected to full medical history, thorough clinical examination and laboratory investigations such as complete lipid profile, fasting blood glucose and hemoglobin A1C.

Results: Overweight was reported in 19.5% of hemophilia patients and obesity in 14.9%. High blood pressure, increase lipid profile (hypercholesterolemia, high LDL, hypertriglyceridemia) and high blood sugar were shown to be more significantly higher in the cases compared to the control group.

Conclusion: Findings from our study revealed hyperlipidemia among people with hemophilia (PwH). Hyperlipidemia, being overweight or obese, and their implications must be prevented and managed early in healthcare for the hemophilia population if it is to improve overall health.

Keywords: Hemophilia, Hypertension, Lipid profile, Obesity, Risk factor.

INTRODUCTION

For people with hemophilia A or B, a lack of clotting factors VIII or IX causes a lifelong bleeding disease. Bleeding can occur with or without trauma in many coagulopathies, and treatment requires therapeutic or preventative replacement of the deficient clotting factor ⁽¹⁾. The more severe the hemophilia, the more likely it is that a person will experience a bleed. Severe hemophilia can result in spontaneous bleeding, abnormal bruising or bleeding, and re-bleeding following invasive procedures (all of these are examples of severe hemophilia) ⁽²⁾.

Joints are the site of approximately 60% of all bleeding events. It is most frequent to have bleeding in one of the following joints: knees. But it can happen in any of the other ones: ankles, shoulders, and wrists ⁽³⁾. Risk factors for mortality and morbidity in hemophilia patients include diabetes mellitus (DM), hypertension (HT), obesity, as well as family history of cardiovascular disease (CVD) ⁽⁴⁾.

Arthritis, functional disability, and chronic joint discomfort are all symptoms of hemophilia. As a result, obesity is a health problem for people with hemophilia (PwH) and a factor exacerbating cardiac, metabolic, and joint health for those who are already predisposed to obesity ⁽⁵⁾. An increase in chronic pain and decreased joint range of motion are all linked to PwH being overweight. A patient's overall health, including their anxiety and distress as a result of their long-term sickness, may be affected by the burden of obesity and hemophilia-related

diseases ⁽⁶⁾. Comorbidities that affect hemophilia care, such as obesity and overweight, may be better addressed with advancements in treatment ⁽⁷⁾.

Atherosclerosis in both children and adults has been linked in several studies to plasma cholesterol levels⁽⁸⁾. Thus assessing changes in lipid profile levels in hemophilic patients is useful in children who requires lifelong therapy ⁽⁹⁾.

Aim of the work was to investigate hemophilia patients for lipid profile changes and its clinical impacts.

PATIENTS AND METHODS

This is a case control study conducted during the period from July 2021 to January 2022, at Pediatric Hematology – Oncology Units (Pediatric Hospital) and Pediatric Hematology Outpatient Clinic at Zagazig University Hospitals, on 153 subject divided into 87 Patients with clinical and laboratory diagnosis of hemophilia (65 hemophilia A and 22 hemophilia B) and 66 age and sex matched healthy children as a control group.

Patients with age <6 and >18 year, with bleeding disorders rather than hemophilia, with genetic or systemic causes for dyslipidemia or patients whose relative refused to participate in the study were excluded from the study.

All participants of the study were subjected to:

A) Complete history taking; with stress on age of diagnosis, inability to move the damaged joint or the

presence of previous bleeding symptoms such as hemarthrosis, muscle hematoma.

- B)** Complete clinical examination including assessment of exercise and nutritional status, blood pressure measurement and anthropometric measurements (body weight and height, body mass index (BMI)⁽¹⁰⁾, waist circumference and waist to height ratio).
- C)** Laboratory investigations:

Lipid profile assessment:

After fasting for 12 hours, a blood sample was collected in the early morning. Samples were centrifuged for 10 minutes at 3,000 g to separate the serum after clotting.

An enzymatic colorimetric technique was used to measure the TG and TC concentrations in the blood. Antibodies were used to block low density lipoprotein (LDL), very low density lipoprotein (VLDL), and chylomicrons, and then the HDL content was determined using a photometric approach. Similarly, after blocking HDL, VLDL, and chylomicrons, enzymatic colorimetric assays were used to quantify LDL.

Fasting blood glucose:

It was assayed by direct method on BS-100 (Shenzhen Mindory Bio-medical Electronics, China).

Assay of hemoglobin A1C.

Ethical consent:

According to the 1964 Declaration of Helsinki and its later revisions or comparable ethical standards, the current study was approved by the Zagazig University Research Ethics Committee (IRB) and conducted in compliance with the ethical standards. Informed consent was obtained from patients' legal guardians before enrollment.

Statistical analysis

The collected data were coded, processed and analyzed using the SPSS (Statistical Package for the Social Sciences) version 22 for Windows® (IBM SPSS Inc, Chicago, IL, USA). Data were tested for normal distribution using the Shapiro Wilk test. Qualitative data were represented as frequencies and relative percentages. Chi square test was used (χ^2) to calculate difference between two or more groups of qualitative variables. Quantitative data were expressed as mean \pm SD (Standard deviation). Independent samples t-test was used to compare between two independent groups and one-way ANOVA test was used to compare more than 2 groups of normally distributed variables (parametric data). P value < 0.05 was considered significant.

RESULTS

The age of the studied groups ranged between 7-18 years with mean of 13.76 ± 3.56 years and 13.67 ± 3.26 years in patients and control respectively (Table 1).

Table (1): Demographic data of the studied groups

Variable		Hemophilia A (n=65)		Hemophilia B (n=22)		Control (n=66)		P
Age: (years)	Mean ± Sd	13.73±3.51		13.79±3.52		13.67±3.26		>0.05
	Range	7-18		7-18		7-18		
		No	%	No	%	No	%	
6 - < 12 years		23	35.38	8	36.36	23	34.8	>0.05
>12 – 18 years		42	64.62	14	63.64	43	65.2	

Sd: Standard deviation

There was a statistical significant increase in weight, height, BMI, and waist circumference among cases with hemophilia compared to control group, but no statistical significant difference was found as regards systolic or diastolic blood pressure (Table 2).

Table (2): Anthropometric measurements and blood pressure of the studied groups

Variable		Hemophilia A (n=65)	Hemophilia B (n=22)	Control (n=66)	P
Weight (kg)	Mean \pm Sd	50.1 ± 21.51	49.83 ± 22.26	38.11 ± 18.47	$<0.05^*$
Height (cm)	Mean \pm Sd	151.65 ± 22.25	151.13 ± 22.38	138.82 ± 24.46	$<0.05^*$
BMI (kg/m ²)	Mean \pm Sd	23.25 ± 6.13	22.98 ± 6.42	19.82 ± 5.47	$<0.05^*$
Waist circumference (cm)	Mean \pm Sd	75.12 ± 13.25	74.67 ± 13.14	67.33 ± 9.18	$<0.001^{**}$
SBP (mmHg)	Mean \pm Sd	112.59 ± 13.86	113.12 ± 12.56	111.67 ± 7.56	>0.05
DBP (mmHg)	Mean \pm Sd	77.88 ± 10.71	77.88 ± 10.71	76.82 ± 8.26	>0.05

Sd: Standard deviation, *: Significant, **: Highly significant There was a statistical significant increase in blood sugar, HbA1C, cholesterol, LDL and triglyceride among cases group compared to control group, while HDL showed non-significant differences (Table 3)

Table (3): Lipid profile of the studied groups

Variable		Hemophilia A (n=65)	Hemophilia B (n=22)	Control (n=66)	P
Blood sugar (mg/dl)	Mean ± Sd	116.98±21.89	117.18±21.59	88.03±3.93	<0.001**
HbA1C (%)	Mean ± Sd	5.28±0.51	5.31±0.53	4.03±0.47	<0.001**
Cholesterol (mg/dl)	Mean ± Sd	172.82±39.07	173.12±40.11	115.39±4.5	<0.001**
LDL (mg/dl)	Mean ± Sd	101.02±7.61	100.92±8.01	60.48±5.94	<0.001**
HDL (mg/dl)	Mean ± Sd	44.09±7.32	43.86±7.29	43.17±3.89	>0.05
Triglyceride (mg/dl)	Mean ± Sd	131.02±5.73	130.38±5.63	58.74±8.69	<0.001**

Sd: Standard deviation, **: highly significant

There was significant difference between hemophilia A patients and hemophilia B patients as regard overweight and obesity (Table 4).

Table (4): Prevalence of overweight and obesity in hemophilia cases

Variable		Hemophilia A (n=65)	Hemophilia B (n=22)	P
Overweight	Number	13	4	>0.05
	Percentage	20	18.18	
Obesity	Number	10	3	>0.05
	Percentage	15.4	13.6	

There was no significant difference in lipid profile data of obese cases in hemophilia A and B groups (Table 5)

Table (5): lipid profile of obese cases in hemophilia A and B

Variable		Hemophilia A (n=10)	Hemophilia B (n=3)	P
Cholesterol (mg/dl)	Mean ± Sd	224.5±17.5	219.5±16.1	>0.05
LDL (mg/dl)	Mean ± Sd	138.5±15.5	134.03±24.1	>0.05
HDL (mg/dl)	Mean ± Sd	47.8±4.9	43.97±3.6	>0.05
Triglyceride (mg/dl)	Mean ± Sd	163.7 ± 6.8	160.38±5.63	>0.05

Sd: Standard deviation

DISCUSSION

It's only been recently that hemophiliacs' risk for cardiovascular and metabolic disease has been identified. There is a lack of research in this field for patients with hemophilia (PwH) ⁽¹¹⁾. Cardiovascular disease mortality and risk assessment has become an issue for hemophilia patients as life expectancy increases. The prevalence of cardiometabolic risk factors, particularly among boys and young men, has been linked to severe obesity in children and young adults ⁽¹²⁾. Arthropathy, functional disability, and chronic discomfort are all symptoms of hemophilia. A person's ability to maintain a healthy weight may be hindered by these impediments to exercise. PwH are more likely to be obese, and this poses a health risk to their hearts, metabolism, and joints ⁽⁵⁾.

Regarding the anthropometric measurements of the studied groups, the current study showed that there was a statistically significant increase in weight, height, BMI and waist circumference among cases compared to control group. However, the study by **Yildiz et al.** ⁽¹³⁾ reported that PwH and controls had no difference in

weight, height, BMI, or waist circumference in children under the age of 18, but in adults, the cases group had a considerably higher weight than the controls. The contrast with our results may be due to the variation in sample characteristics. Also, the study by **Özdemir et al.** ⁽¹⁴⁾ reported that there was no statistically significant difference in weight, and BMI among cases compared to control group. While the study by **Kazemi et al.** ⁽¹⁵⁾ reported that the mean BMI was significantly lower in patients with hemophilia than control.

As regards the frequency of obesity among the studied groups, we found that obesity was more common in patients compared to controls, which was statistically significant. Overweight was reported in 19.5% of our hemophilia patients and obesity in 14.9%. Our results were supported by **Yildiz et al.** ⁽¹³⁾ who reported that no kids younger than 10 had obesity, 7.7 percent of patients between 10 and 18 and 25 percent of PwH between 18 and 40 years old had obesity.

Our results showed that there was no statistical significant difference between the studied groups in

systolic or diastolic blood pressure. These data were in agreement with **Yildiz et al.** ⁽¹³⁾ and **Kazemi et al.** ⁽¹⁵⁾ who reported that there was no statistical significant difference between the studied groups regarding hypertension. On contrast in a study by **Foley et al.** ⁽¹⁶⁾, hemophilia patients had greater blood pressure than the general population. Fifty percent of PwH above the age of 18, compared to 23 percent of those under the age of 18, had high blood pressure and heart rate (BP/HT) ($p=0.03$). In the hemophilia group, the frequency of raised BP/HT was greater than in the control group, although not statistically significant. (35.5% vs. 28.6%, $p=0.51$) ⁽¹⁷⁾.

Regarding laboratory results of the studied groups, we found that there was a statistically significant rise in blood sugar, HbA1C, cholesterol, LDL, and triglycerides in hemophilia cases compared to control group while HDL showed non-significant differences. Hyperlipidemia was shown to be more common in hemophiliacs (15.9%) compared to healthy people in a large US cohort research (11.9 percent) ⁽¹⁸⁾. However, the study by **Yildiz et al.** ⁽¹³⁾ reported that fasting glucose and triglyceride increased in patients compared to controls, although fasting insulin, HOMA-IR and lipid profile were equivalent in the examined groups.

Furthermore, **Kazemi et al.** ⁽¹⁵⁾ found that there was no statistical significant difference between the two groups; fasting insulin, HOMA-IR, total cholesterol, LDL, HDL and Uric acid were comparable in the studied groups. As well, there was no statistical significant difference between the studied groups regarding FBS, HDL but cholesterol, TG and LDL were significantly higher in patients as compared to controls. Also, the study by **Sun et al.** ⁽¹¹⁾ reported that there was no statistical significant difference between the studied groups regarding homocysteine, cholesterol, LDL, HDL and TG. This can be supported by **Sood et al.** ⁽¹⁸⁾ as they reported that hemophilia type was not correlated with the prevalence of dyslipidemia and CVD.

The variation in the results between the studies was due to the differences of the inclusion and exclusion criteria.

CONCLUSION

Findings from our study reveal a high prevalence of abnormal lipid profile among PwH. Hyperlipidemia, being overweight or obese, and their associated repercussions must be prevented and managed early in healthcare for the hemophilia population in order to improve overall health.

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