Hemophyliacs profile from a patients' association in Brasília - DF, Brazil

Perfil dos hemofílicos de uma associação de pacientes de Brasília – DF, Brasil

Perfil hemofílico de una asociación de pacientes en Brasília - DF, Brasil
Perfil de pacientes hemofílicos em Brasília, Brasil

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RESUMO

Objetivo: Caracterizar o perfil de hemofílicos vinculados a uma associação de pacientes em Brasília - DF, Brasil. **Método:** Pesquisa transversal com amostragem por conveniência, realizada com 49 hemofílicos adultos, do sexo masculino, vinculados à Associação dos Voluntários, Pesquisadores e Portadores de Coagulopatias (AJUDE-C). O estudo foi aprovado pelo Comitê de Ética em Pesquisas com Seres Humanos. Através de um formulário foi coletado informações sociodemográficas e clínicas. A normalidade dos dados foi avaliada através do teste de Shapiro-Wilk. **Resultados:** Avaliaram-se 49 hemofílicos adultos com média de idade 37 ±8,4 anos, estando 43% na faixa etária de 30-39 anos. Predominou a raça/cor parda (49%), estado civil solteiro (61%), em atividade laboral (57%) e 53% residiam a menos de 30 Km do local de tratamento. Clinicamente, predominou a hemofilia A (79,6%), doença grave (77,6%) e o uso de profilaxia secundária (75,5%). **Conclusão:** Maior parte da amostra exerce atividade laboral. Esse fato pode ser explicado pela administração da profilaxia secundária e proximidade entre a residência/local de tratamento, mantendo os fatores de coagulação em níveis seguros, e dando capacidade de rápido atendimento em casos emergenciais, gerando maior autonomia nessa população.

Descritores: Hemofilia; Distúrbio de coagulação; Profilaxia.

ABSTRACT

Objective: To characterize the hemophiliacs profile linked to a patients association in Brasília - DF, Brazil. **Method:** Cross-cut survey with convenience sampling, carried out with 49 male hemophiliacs adults, linked to the Association of Volunteers, Researchers and People with Coagulopathies (AJUDE-C). The study was approved by the Ethics Committee in Research with Human Beings.The Sociodemographic and clinical information was collected through a form. The normality of the data was evaluated using the Shapiro-Wilk test. **Results:** Were evaluated 49 adult male hemophiliacs with an avarage 37 ± 8.4 years. 43% were in the 30-39 age range. The brown race predominated (49%), single marital status (61%), in work activity (57%) and 53% lived less than 30 km from the treatment place. Clinical prevalence hemophilia A (79.6%), severe disease (77.6%) and the use of secondary prophylaxis (75.5%). **Conclusion:** Most of the sample is in work activity. This fact can be explained by the administration of secondary prophylaxis and proximity between their residence / treatment place. This keeps the clotting factors at safe levels, and provids quick assistance to emergencies cases, generating greater autonomy in this population.

Descriptors: Hemophilia; Coagulation disorder; Prophylaxis.

RESUMEN

Objetivo: Caracterizar el perfil de hemofílicos vinculados a una asociación de pacientes en Brasilia - DF, Brasil. **Método:** Encuesta transversal con muestra de conveniencia, realizada con 49 hemofílicos adultos, vinculados a la Asociación de Voluntarios, Investigadores y Personas con Coagulopatías (AJUDE-C). El estudio fue aprobado por el Comité de Ética y Investigación en Seres Humanos. La información sociodemográfica y clínica se recogió por medio de un formulario. La normalidad de los datos se evaluó mediante la prueba de Shapiro-Wilk. **Resultados:** se evaluaron 49 hemofílicos adultos con una edad media de 37 ± 8,4 años, 43% estaban en el grupo de edad 30 a 39 años. Predominó la raza marrón (49%), estado civil soltero (61%), en la actividad laboral (57%) y el 53% vivía a menos de 30 km del sitio de tratamiento. Clínicamente predominaron: hemofilia A (79,6%), enfermedad grave (77,6%) y el uso de profilaxis secundaria (75,5%). **Conclusión:** La mayor parte de la muestra tiene actividad laboral. Este hecho puede explicarse por la administración de profilaxis secundaria y la proximidad entre el lugar de residencia / tratamiento, manteniendo los factores de coagulación en niveles seguros y promoviendo la capacidad de atender rápidamente los casos de emergencia, generando una mayor autonomía en esta población.

Descriptores: Hemofilia; Trastorno de la coagulación; Profilaxis.

ORIGINAL

Introduction

Hemophilia is an inherited hemorrhagic disease linked to the X chromosome, characterized by the deficiency or abnormality of factor VIII (hemophilia A) or factor IX (hemophilia B) coagulant activity. Hemophilia is transmitted almost exclusively to male individuals by mothers carrying the mutation (about 70% of cases).[1]

The incidence of hemophilia A is approximately 1: 10,000 to 1: 30,000 births, while hemophilia B is 1: 30,000 to 1: 50,000. Both have the same clinical presentation, making it necessary to measure the activity of specific coagulation factors, factor VIII and factor IX, to differentiate between them.[2]

The Society for Thrombosis and Hemostasis classifies the severity of hemophilia based on endogenous Factor VIII or IX activity as severe (<1 IU / dL), moderate (1-5 IU / dL) or mild (> 5-40 IU / dL), all three with a specific phenotype. Patients with severe hemophilia (approximately 40% of hemophiliacs) have spontaneous or soft tissue and joint bleeding, causing arthropathy, impaired quality of life and increased risks of intracranial hemorrhage or early death. Patients with moderate hemophilia, in contrast, are less affected, but suffer, for example, from prolonged bleeding or bruising. Patients with mild hemophilia only experience bleeding problems during and after trauma or surgery.[3]

Prophylactic replacement of the clotting factor is the most effective preventive measure against joint bleeding. It has been well demonstrated that the later the first bleeding, the less severe the arthropathies are, supporting the need for preventive treatment to begin in early childhood. The coagulation factor can be obtained from human plasma or manufactured synthetically by genetic engineering technologies - the so-called recombinant factor. Studies show that the success rate of the recombinant factor is 90% higher than the plasma.[4]

The development of neutralizing antibodies (inhibitors) against factor VIII or factor IX is the most serious complication of the treatment of hemophilia, occurring in 20% - 30% of patients with severe hemophilia A, 5% -10% in patients with hemophilia classified as mild to moderate and less than 5% in patients with severe hemophilia B. These antibodies make replacement therapy ineffective, with a consequent increased risk of severe bleeding and early onset of progressive arthropathy, as well as higher treatment-related costs.[5]

The Midwest has the lowest number of patients in the country, totaling 982 hemophiliacs of types A and B, however the Federal District shows an increase in the expected prevalence for both hemophiliacs (1.9 / 10,000 men) 2. Thus, the objective was to characterize the profile of hemophiliacs linked to a patient association in Brasília - DF, Brazil.

Method

This is a transversal and analytical research, with a quantitative approach. Convenience sampling, performed with patients with a clinical diagnosis of hemophilia linked to the Association of Volunteers, Researchers and People with Coagulopathies (AJUDE-C), located in Brasília - DF.

Patients with a clinical diagnosis of hemophilia (ICD 10 - D. 66 and D. 67), male, over 18 years of age were included. Associated with other coagulopathies and / or with some cognitive or physical impairment that prevented them from responding to the research protocol were not included.

Data collection was carried out at the AJUDEC association, in Brasília - DF, in the months of November and December 2019. The research team attended meetings and events at the said association on two previously informed dates. On these occasions, an individual invitation was made to patients, briefly explaining the research. Then, the Free and Informed Consent Form (ICF) was submitted for appreciation and signature. This term was signed in two copies, one for the patient's possession and the other for the research team.

In case of consent by the patient, the research protocol was subsequently applied, individually and privately.

The research protocol consisted of an instrument, developed by the research team, which aimed to collect sociodemographic information (age, race/color, marital status, employment status, distance between residence / place of treatment) and clinics (type of hemophilia, severity type of treatment).

For the organization and analysis of the data, a database was created in the Excel program. The results of this study were presented in the form of descriptive statistics or in the form of tables and graphs. The statistical analysis was performed using the SPSS statistical program, version 22.0, considering a significance level of 5%. The Shapiro-Wilk test assessed the normality of the data.

In compliance with CNS Resolution 466/12, all instruments completed during data collection will be kept in a physical file for a period of 5 years after the end of the study, under the responsibility of the responsible researcher. The study was approved by the Ethics Committee on Research with Human Beings, under opinion 1,300,316.

Results

49 adult hemophiliacs with a mean age of 37 ± 8.46 years were evaluated, with 43% in the 30-39 year age group. The race / brown color predominated (49%), single marital status (61%), with work activity (57%) and 53% lived less than 30 km from the treatment site. Clinically, there was a predominance of hemophilia A (79.6%), with severe clinical classification (77.5%) and use of secondary prophylaxis (75.5%). Sociodemographic characterization was performed as shown in Table 1.

Table 1- Sociodemographic information, of hemophiliacs evaluated in this study.

Age Range (years)	**% (n=49)**
20-29	18
30-39	43
40-49	31
50-59	8
Mean Age	37±8,46
Marital Status	**% (n=49)**
Singles	61
Married	39

Color / Ethnicity	% (n=49)
White	39
Brown	49
Black	12
Education Level	**% (n=49)**
Incomplete 1st Degree	6,12
1st Degree Complete	2
2nd Grade Incomplete	4
2nd Degree Complete	24,5
Incomplete 3rd Degree	20,4
3rd Degree Complete	42,9
Health Insurance	**% (n=49)**
Yes	47
No	53
Government Benefit / Financial Aid	**% (n=49)**
Yes	29
No	71
Distância da Residência ao Local de Tratamento	**% (n=49)**
Less than 30 Km	53
More than 30 Km	47

Table 2 shows the data referring to the characterization of hemophiliacs in relation to their work characteristics, developed physical activities and BMI.

Table 2- Profile of Work Activity, Physical Activity and Body Mass Index of Hemophiliacs.

Labor Activity	**% (n=49)**
Yes	57
No	41
Uninformed	2
Physical activity	**% (n=49)**
Yes	63
No	37
Body mass index	**% (n=49)**
Eutrophic	42,86
Overweight	42,86
Obesity	12,24
Low Body Mass	2

Table 3 presents the characteristics of the treatment and their therapeutic options.

Table 3-Characterization of hemophilia and treatments.

Virus Infection	**% (n=49)**
Hepatitis C	46,94
Not	44,9
Hepatitis B and C	4,08
Hepatitis C and HIV	4,08
Treatment Type	**% (n=49)**
P1	0
P2	75,5
P3	12,25
Demand	12,25
Type HF	**% (n=49)**
A	79,6
B	20,4
Gravity	**% (n=49)**
Serious	77,5
Moderate	18,4
Light	4,1
Inhibitor	**% (n=49)**
No	95,9
Yes	4,1

Legend: P1 - Primary prophylaxis; P2 - Secondary prophylaxis; P3 - Tertiary prophylaxis; Type HF - Type of hemophilia.

Discussion

The average age of the individuals was 37 ± 8.4 years, with the age group of 30 to 39 years having a higher prevalence, with 43% of the sample. Similar results were found in research developed by Booth et al. (2018)[6] using data from 1225 adult hemophiliac patients (≥18 years old), from five European countries: France, Germany, Italy, Spain and the United Kingdom, where the average age presented was 35.5 years. However, the Profile of Hereditary Coagulopathies (Brazil, 2018)[2], shows that there is a higher concentration of Brazilian hemophiliacs in the age group of 20 to 29 years, differing with the results found.

As for the marital status of the participants, there was a higher prevalence of singles (61%). Naous et al. (2019)[7] conducted a survey where 66.7% of individuals were also single. In the same study, 78.3% of individuals declare that they have no difficulty in talking about the disease to others, suggesting some transparency in their social life.

In the present study, 49% of individuals were brown, 39% white and 6% black. According to the 2010 demographic census of the Brazilian Institute of Geography and Statistics (IBGE), stratified by the age and estimated sex of the male population residing in the Federal District (1,161,048), 49.3% of individuals were brown, 42.2% were white and 8.5% black; a consistency with the ethnic distribution of Brasilia is observed. According to Kelley and Narváez (2006)[8], hemophilia affects predictably all ethnic groups and races, regardless of the

country.

As for the level of education, there was a predominance of individuals with complete higher education (42.9%). However, divergent results were presented by Moreno and Buitrago (2017)[9], where 68.3% of hemophiliacs had completed high school, taking into account that in this sample the age range was 18 to 82 years. Cutter et al. (2017)[10] suggest that the reasons for low education are school absenteeism, caused by bleeding or pain (69%), difficulties in attending school or participating in activities resulting from impaired mobility (44%), and absences related to hemophilia (32%).

The results of this study show that 53% of hemophiliacs did not have health insurance, and 71% did not receive any kind of benefit. A study carried out in Indiana (USA) with a sample of 704 hemophiliacs showed that 89.2% of the studied population had insurance during the study period.[11]

About 53% of hemophiliacs lived less than 30 km from the treatment site. These results are explained by Sousa et al. (2013)[12], noting that a smaller geographical distance between home and place of treatment can facilitate emergency care in case of bleeding.

Of the 49 individuals assessed, 63% were engaged in physical activity and 57% engaged in work activity, and 2% of the sample did not report in relation to work activity. Regarding physical activity Flaherty et al. (2017)[13] observed that hemophiliac patients who exercised regularly did not consider exercise dangerous, while those who did not exercise reliably, feared that the dangers of exercise might outweigh the benefits. Results indicate that, despite arthropathy and thanks to prophylactic treatment, adult patients with hemophilia are able to perform physical activities with a minimal risk of bleeding.[14]

Cutter et al. (2017)[10] showed similar results regarding work activity, where most individuals with hemophilia worked (81%). In this same study it was found that adults with hemophilia who had never worked were younger (<30 years, 73% vs 30-45 years, 20%), in addition, more than half (59%) of adults with hemophilia declare that the reason they were not working involves financial reasons related to hemophilia (for example, receiving disability benefits), and 55% reported to be due to hemophilia and its related complications (joint disease).

Regarding the body mass index (BMI), the sample was divided into eutrophic patients (42.86%), overweight (42.86%), obese (12.24%) and low body mass (2%) . Buckner et al. (2018)[15], with a sample of 381 adult hemophiliac men, observed that most individuals were overweight or obese (65%). In the present study, anthropometric measurements did not affect the number of bleeds.

In research developed by Targino Júnior et al. (2017)[16], no significant differences were found in any component of body composition (lean mass, fat mass, visceral fat) and in anthropometric indices (waist-to-hip ratio [WHR]), BMI and visceral fat of hemophiliacs.

Regarding the clinical characterization of the sample, the result of this study showed that hemophilia A was more prevalent than B, with 79.6% and 20.4% respectively. It is estimated that hemophilia A is more common than hemophilia B, and represents about 80% of cases.[2] Similar results were found in the study by Ferreira et al. (2018)[17], where the most frequent type was hemophilia type A with 82%, followed by 10% hemophilia B and 8% with von willebrand disease (DWW). Pérez-Moreno and Buitrago (2017)[9] found 79% of cases of

hemophilia A in a population of 196 participants.

The classification of the clinical severity of hemophilia is carried out according to the plasma level of factor VIII or factor IX and hemorrhagic manifestations.[1] In this study, it was observed that most cases were severe (77.5%), followed by 18.4% moderate and 4.1% mild. Similar results were found by Martinez-sanchez et al. (2017)[18], where there was a predominance of the severe type with 55.6%, moderate (22.2%) and mild (22.2%).

The main current complication in the treatment of hemophilia is the development of inhibitory antibodies against factor VIII or factor IX.[2] In the literature, the incidence of the development of inhibitors is reported in 25% to 30% of patients with severe Hemophilia A and up to 10% in those with severe Hemophilia B.[19] In the present study, of the 49 patients questioned, 79.6% are hemophiliacs with severe clinical classification, however 95.9% did not develop inhibitors, the results being below this statistic.

Among the patients, 55.1% had some type of viral infection, with 46.94% acquiring hepatitis C, 4.08% hepatitis B and C and the others, 4.08% Hepatitis C and HIV. In a study developed by Lianes et al. (2018)[20], with a sample of 34 hemophiliacs, they observed that 30 of these (88.2%) had antibodies against HCV by (EIA-3) UMELISA-HCV, while HCV-RNA infection was obtained in 23 patients (67.6%). Coinfection with the hepatitis B virus was found in 2 patients (5.8%) and the same percentage for the human immunodeficiency virus (HIV). Makris and Konkle (2017)[21] reported that co-infection with the hepatitis C virus makes the hemophiliac patient more likely to develop cancer or liver failure decades after infection, in addition, previous studies have shown that from 20 to 30% of infected patients, develop terminal liver disease. Current data reported in the European Hemophilia Safety Surveillance Program (EUHASS) up to 2015 further show that hepatocellular cancer is the most common cancer in patients with hemophilia, and liver disease is the most common cause of death in these individuals.

In this study, it was observed that 75.5% use secondary prophylaxis treatment, in which the main pillar is the replacement of the deficient coagulation factor.[2] Castaño et al. (2017)[22] also showed that almost all (96.6%) patients in their sample were being treated with prophylaxis, and also reported that the hemophiliacs who adhered to this treatment have a quality of life as high as the general population. Lianes et al. (2018)[20] emphasize that the concentrate of factors is considered the gold standard in this type of treatment. In addition, the same proved to be positive, where primary and secondary prophylaxis had advantages in the results of the following variables: pain, functionality, quality of life, recovery time measures, return to normal activities, orthopedic intervention, bleeding measures, and sustained productivity.

Conclusion

The sociodemographic and clinical characterization described in the present study shows that part of the patients was born in a period of great contagion due to infectious diseases through blood products, and more than half (55.1%) presented some type of viral infection, which increases morbidity and mortality in this population. The sample consisted mainly of adults who work and have completed higher education. This fact can be explained by the

administration of secondary prophylaxis, and proximity between the residence/place of treatment, keeping the clotting factors at safe levels, providing the capacity for rapid care in emergency cases and generating greater autonomy in this population.

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