ARTÍCULO ORIGINAL

Prevalence of hemophilia in six cuban provinces

Prevalencia de hemofilia en seis provincias cubanas

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ABSTRACT

Introduction: hemophilia is an inherited bleeding disorder; its incidence is almost constant in different populations. Since the 80th decade a multidisciplinary group for the care of patients with hemophilia was created at the Instituto de Hematología e Inmunología. Nowadays a national comprehensive care program allows patients to receive a continuous monitoring and an effective treatment.
Objective: to know prevalence of patients with hemophilia in Cuba.
Results: data of 229 patients from 5 provinces and the special municipality Isla de la Juventud were included, which covered 58.71 % of the total patients registered in Cuba. The information included demographic data, severity of hemophilia, presence of inhibitors and infection status for viral diseases. Hemophilia A patients were 188 (82.10 %) and 41 (17.90 %) with hemophilia B. The disease was severe in 56.33 % of patients, moderate in 24 %, and mild in 19.70 %. Inhibitors were present in 17.03 % of the patients. Human immunodeficiency virus infection was present only in 0.87 % of patients and hepatitis C virus infection in 39.03 %. The mean age at diagnosis was 2.15 years.
Conclusions: the general age-adjusted prevalence was 9.63 cases of hemophilia per 100 000 male and the main prevalence of patients was found in ages between 20 and 59 years.

Keywords: hemophilia, epidemiology, prevalence, Cuba.

RESUMEN

Introducción: la hemofilia es una enfermedad hemorrágica con una incidencia casi constante para diferentes poblaciones. Desde la década del 80 del pasado siglo, en el Instituto de Hematología e Inmunología se creó un grupo multidisciplinario de especialistas para la atención del paciente con hemofilia. En la actualidad existe un programa nacional de atención integral al hemofílico que permite el monitoreo continuo y el tratamiento adecuado.
Objetivo: conocerla prevalencia de la hemofilia en Cuba.
Métodos: se incluyeron los datos de 229 pacientes procedentes de 5 provincias cubanas y el municipio especial Isla de la Juventud (según la división política-administrativa previa), que representan el 58,1 % de los pacientes registrados.
Los datos incluyeron aspectos demográficos, gravedad de la enfermedad, presencia de inhibidores y de infecciones transmitidas por las transfusiones.
Resultados: los pacientes con hemofilia A fueron 188 (82,10 %) y 41 (17,90 %) con hemofilia B. El 56,33 % de los pacientes presentaron la enfermedad en forma severa, 24 % moderada y 19,7 % leve. Los inhibidores se encontraron en el 17,03 % de los casos. La infección por el virus de inmunodeficiencia humana estuvo presente solamente e el 0,87 % de los pacientes, y la hepatitis C en el 39,03 %. La edad media al diagnóstico fue de 2.15 años.
Conclusiones: la prevalencia general ajustada a la edad fue de 9,63 casos de hemofilia por 100 000 varones y la mayor prevalencia de pacientes se encontró en las edades entre 20 y 59 años.

Palabras clave: hemofilia, epidemiología, prevalencia, Cuba.

INTRODUCTION

Hemophilia is bleeding disorder caused by diminish of procoagulant activity of factor VIII or IX. The incidence is almost constant in different populations. It is the second most common genetic bleeding disease after von Willebrand disease (VWD), and the most common hereditary entity linked to chromosome X.

The complications of this disease are diverse, ones given by serious bleeding events that may occur, such as frequent joint bleeds causing permanent joint damage that leads the patient to a physical disability; and others such as the presence of inhibitors and infectious diseases transmitted through blood transfusion products.

Since the 80th decade of the 20th century, a multidisciplinary group was created at the Institute of Hematology and Immunology, La Habana, Cuba, for the care of patients with hemophilia (PWH). This group was formed by hematologists, orthopedists, laboratory technicians and psychologists. Gradually, other specialists joined the group and at present a national comprehensive care program has been developed whichallows patients to receive a continuous monitoring and an effective treatment.[1]

This is the first report that includes demography and epidemiology data in our country with characterized PWH from different provinces. The main objective of this cross-sectional study was to provide information about the present situation of hemophilia A (HA) and hemophilia B (HB) in Cuba.

METHODS

Data on 229 patients from 5 provinces (according to previous political administrative distribution): Ciudad de La Habana, La Habana, Pinar del Río, Matanzas, Cienfuegos and special municipality Isla de la Juventud, were collectedin the period from January 2007 to December 2010. Information included demographic data, severity of hemophilia, presence of inhibitors and infection status for viral diseases.We defined the haemophilia severity following the classification of the International Society on Thrombosis *&* Haemostasis (ISTH), mild (5-40 %), moderate (1-5 %) and severe (< 1 %).[2] The information was collected in a database created for this research, called HEPIGENET (hemophilia genetic epidemiology). We estimated the prevalence rate of hemophilia A and B (per 100 000 males) by provinces and age group, using EPIDAT 3.1 statistical program. The 95 % confidence limits for reliability were calculated for the rate, which was adjusted for age and sex. Frequencies and percentages were used as a summary of measures for qualitative data and their analysis was performed using the Chi square test. Quantitative variables were analysed using the mean, median, percentage and range; also the Kruskal-Wallis test was used for comparison. The level of significance was $p< 0.05$.

RESULTS

The patients studied covered 58.71 % of the total registered in Cuba. HA patients were 188 (82.10 %) and 41 (17.90 %) with HB. The disease was severe in 56.3 % haemophiliacs, moderate in 24 % and mild in 19.7 %. Inhibitors were present in 17.03 % of the patients. The mean age of the hemophiliacs was 31.74 years old (SD ± 17.30).

Distribution of the patients by type of hemophilia, severity of the disease and the prevalence rate in both types of hemophilia in the country and by provinces, is shown in table 1. Patients with HA *&* HB in relation to age are shown in table 2, 27.94 % under 19 years of age. More than half of the population were between 20 and 59 yea old. Within this group, the highest (39.30 %) was between 20-39 years old. In HA, this group represented 38.29 % and in HB, 43.90 %. When we compared both groups the differences were not significant. It is important to point out that we found 12 patients (5.23 %) aged over 60 years and one over 80.

In connection with the prevalence of hemophilia adjusted to the age and the level of severity of the disease, we observed an absolute prevalence of patients between 15 and 40 years old as well as for the severe cases (prevalence rate 23.82 per 100 000 males) and when the cases were pooled the prevalence rate was 26.10 per 100 000 (figure 1).

In figure 2 the compared perceptual distribution of hemophilia population with the overall Cuban male population is observed.The hemophilia population had a much greater proportion of younger males in the ages between 5 and 39. In the rest of the age group the non hemophilia population prevailed.

Table 1. Distribution of patients according to type and severity of hemophilia and prevalence rates in provinces studied

Provinces	HA		HB		Hemophilia A + B						Total	Prevalence
					Severe		Moderate		Mild			
	n	%	n	%	n	%	n	%	n	%		
Ciudad de La Habana	90	76.3	28	23.7	67	56.7	23	19.5	28	23.7	118	11.41
Cienfuegos	3	75.0	1	25.0	4	100	0	0.0	0	0.0	4	1.97
La Habana	31	88.6	4	11.4	16	45.7	13	37.1	6	17.1	35	9.34
Isla de la Juventud	4	100	0	0.0	4	100	0	0.0	0	0.0	4	8.95
Matanzas	26	96.3	1	3.7	13	48.1	8	29.6	6	22.2	27	7.95
Pinar del Río	34	82.9	7	17.1	25	60.9	11	26.8	5	12.2	41	11.0
Six provinces	188	**82.1**	41	**17.9**	129	56.3	55	24.0	45	19.7	229	**9.63**

HA: Hemophilia A HB: Hemophilia B p=0.00

Table 2. Distribution of patients according to age group and type of hemophilia

Age group (years)	Type of hemophilia				Total	
	Hemophilia A		Hemophilia B			
	n	%	n	%	n	%
≤4	5	71.4	2	28.6	7	3.05
5-9	14	87.5	2	12.5	16	6.98
10-14	20	90.9	2	9.1	22	9.60
15-19	14	73.7	5	26.3	19	8.29
20-39	72	80.0	18	20.0	90	**39.30**
40-49	32	86.5	5	13.5	37	**16.15**
50-59	21	80.8	5	19.2	26	**11.35**
60-69	6	75.0	2	25.0	8	3.49
70-79	3	100	0	0.0	3	1.31
80-84	1	100	0	0.0	1	0.43
Total	188	82.1	41	17.9	229	100

p = 0.72

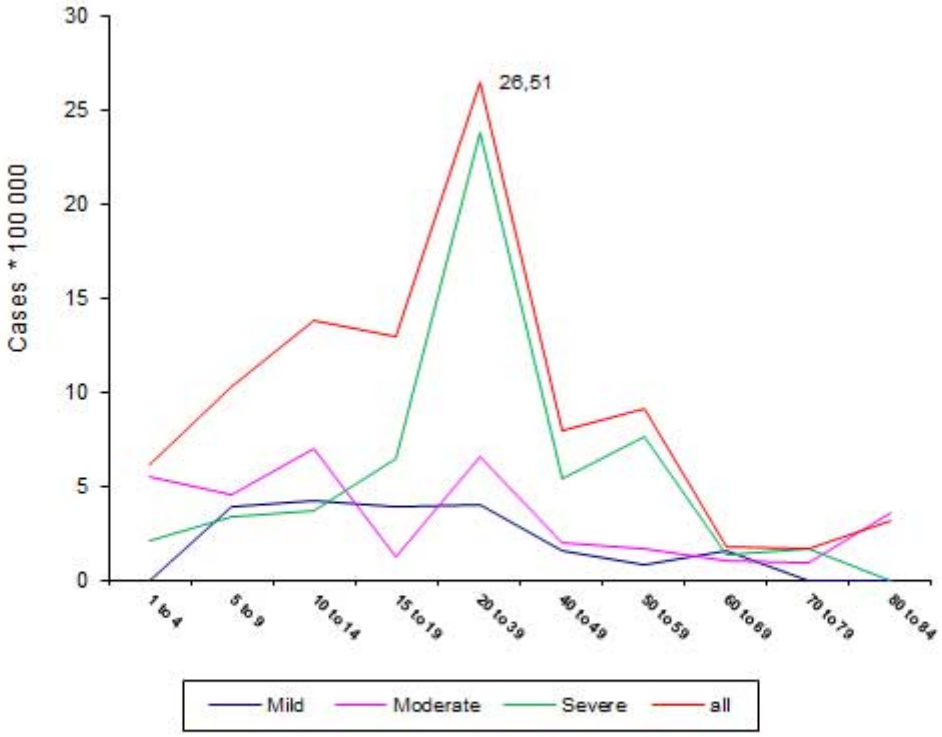

Fig.1. Prevalence of hemophilia adjusted to the age and the level of severity of the disease.

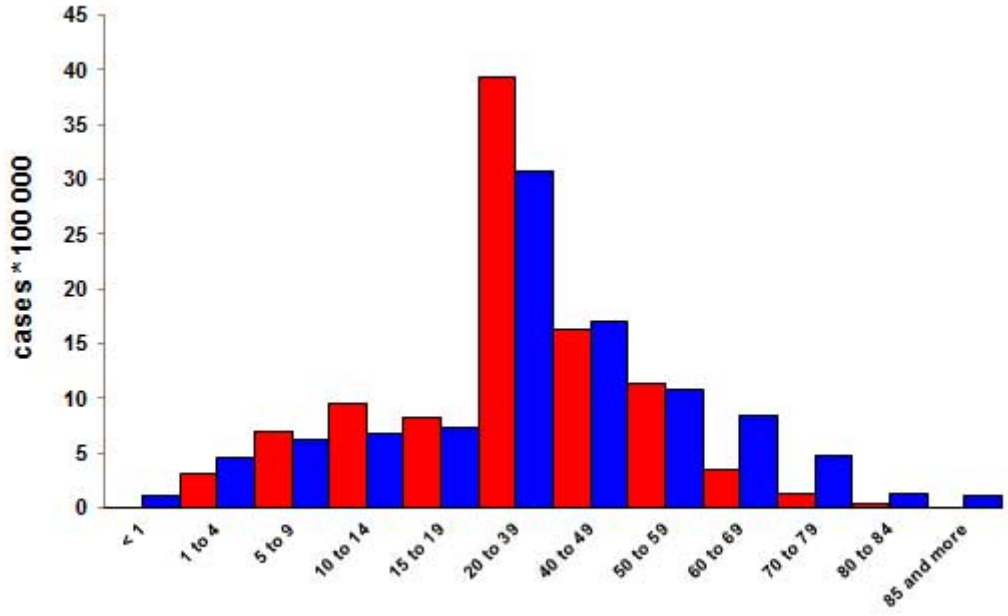

Fig. 2. Distribution by age for persons with hemophilia and residents in Cuba.

Median age for patients diagnosed with mild hemophilia was 3 years for HA and 5 for HB. Regarding moderate disease the median was 2 years old for both types of haemophilia and 3 for HB. The median for severe cases was under one year in both types.

When we analysed the seroprevalence of transmitted transfusion disease, 0.87 % of patients were infected with Human Immunodeficiency Virus (HIV). The patients with Hepatitis C Virus (HCV) were 39.03 %. The infection with Hepatitis B Virus (HBV), co-infection HBV+HCV and HBV/HCV+HIV were underestimated.

DISCUSSION

For many years, the general rates of prevalence in hemophilia were settled down similar for individuals and countries of different latitudes and ethnic groups.[3] The discrepancies found in the diverse researches that broach this topic generally conform to the sub-register observed in many countries where patients with hemophilia have limited access to the Public Health Systems or to specialized institutions.[4]

The proportion of patients with HA and HB were similar in the different reports, but the actual mean ages are different when we compare our results with the ones of other authors. These outcomes are probably influenced by the high mortality of hemophiliacs infected with HIV since the 1980s phenomenon that occurred mainly in developed countries due to their access to substitute therapy without viral process.[5] Our results showed low HIV infection as our patients only received blood products from Cuban donors duly processed; at that moment the seroprevalence of HIV was low in Cuba, whereas in the rest of the world these figures were high.[6]

Regarding the infection of hepatitis C, our results are high, similar to other studies.[7] It is known that the window period of this disease is very long and the hemophilic patients have received these blood components when they were supposed to be safe. This has occurred basically because the developing countries, such as ours, have continued using blood products, plasma and cryoprecipitate, which were not submitted to viral inactivation; while the developed countries were infected in the 80´s. In Cuba, the seroprevalence of hepatitis B is very low because in 1992 vaccination against this virus started which has proven to be safe and immunogenic.[8] Similar low results were found in the co-infection HCV+HBV and HCV+HIV.

We have patients over 60 years of age; although adultPWHhave certain muscle-skeletal limitations, most of themhave aged with favorablehealth status which allows them to maintaina normal social life. This conditionis favoredbythe characteristics of our national health system with national coverage, results of the application of a strategy and deployment of essential public health principles. This favorable condition permits us to compare ours findings with the observed results ininternational reports.

When we analyze the results of reports from European countries and the United States, we observe that more than 15 % of PHW are older than 75-80 years due to the higher level of development of the local Comprehensive Care Programs.[3] It is difficult to find similar figures in the reports of the majority of the under developed countries, because of their deficient systems of health.

Nowadays, there is a National Comprehensive Care Program in Cuba that allow patients to receive continuous monitoring and intends to improve the quality of life for patients with hemophilia.

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