

Challenges and perspectives in the treatment of patients with haemophilia in Brasil

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Dear Editor,

Haemophilia affects more than 184,000 people worldwide.¹ Despite increasing advances, it is still associated with a high prevalence of disabilities, posing an economic burden to individuals and health systems.² Over the last decades, significant therapeutic improvements have been achieved, including advances in blood safety, prophylaxis with coagulation factor concentrates (CFC), treatment with inhibitors of coagulation factors, orthopedic surgeries to correct limbs deformities and long-acting CFC.^{2,3} It is anticipated that new compounds which could be applied subcutaneously and gene therapy will be of benefit to patients with hemophilia (PWH) in the future.⁴

Without prophylactic treatment, approximately 80% of all bleedings in PWH occur inside joints (haemarthroses), mainly ankles, knees and elbows.⁵ Although prophylaxis with CFC for children and adults with severe hemophilia is recognized to prevent hemophilic arthropathy,⁶ it is not available to all PWH. Accordingly, it is estimated that approximate-

ly 75% of PWH worldwide (~350,000) are not regularly treated, if at all.⁴

It is known that CFC accounts for up to 80% of the overall cost of hemophilia treatment² presenting a barrier to patient care in developing countries. Indeed, hemophilia health care costs in the United States are approximately \$140,000 USD/year;⁷ in patients with inhibitors to factor VIII, costs of treatment can be 4.8 times higher.⁷

According to the last Annual Global Survey (Table 1), Brazil has the fourth highest number of registered PWH (n=12,119).¹ The Brazilian federal government provides 100% of CFC to these patients; up to 77% of PWH under 18 years of age and 31% for those over 18 benefit from prophylaxis, although this was only available from late 2011.¹ The Brazilian Unified Health System (SUS), which is part of the 1988 National Constitution, acknowledges that health is a fundamental right of the citizen, which must be guaranteed by the State through a set of

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governmental policies and actions, with community participation (social control).

According to the SUS principles of hierarchy and decentralization, in this context, the roles of the Ministry of Health (MoH) are purchasing the CFCs and establishing national policies and guidelines, while the states and municipalities are responsible for the multidisciplinary care of PWH.

The PWH society encompasses non-governmental organizations (NOG), as well as individuals with inherited bleeding disorders and their relatives. The Brazilian Federation of Haemophilia (FBH), with its regional chapters, represents Brazil in the World

Federation of Hemophilia (WFH); they play a key role in advocating for PWH.

The WFH (through FBH) has been providing the MoH with technical, accessible and credible information on products for the treatment of bleeding disorders and their costs, as practiced in other countries, thus supporting better decision-making by the country. It also conducts national and international meetings as well as scientific congresses, which are important to the development of public policies. Moreover, FBH is represented on the *Coagulopathy Committee*, the technical arm of the MoH in the Bleeding Disorders area. This committee, among

TABLE 1. POPULATION DATA FROM THE FOUR COUNTRIES WITH THE LARGEST NUMBER OF PEOPLE WITH HEMOPHILIA WORLDWIDE, ACCORDING TO THE REPORT ON THE ANNUAL GLOBAL SURVEY 2016 FROM THE WORLD FEDERATION OF HEMOPHILIA, 2017.

Country	Population	People with hemophilia	Haemophilia A		Mean per capita factor VIII use*	Haemophilia B		Mean per capita factor IX use*
India	1,324,171,354	18,353 (756 type unknown)	Age 0 to 4	2%	0,105 (including humanitarian aid)	Age 0 to 4	2%	0,002
			Age 5 to 13	15%		Age 5 to 13	13%	
			Age 14 to 18	11%		Age 14 to 18	13%	
			Age 19 to 44	36%		Age 19 to 44	41%	
			Age ≥45	7%		Age ≥45	9%	
			Age not known	28%		Age not known	22%	
			Total	15,218		Total	2,379	
United States	323,127,513	16,949	Age 0 to 4	9%	9,532	Age 0 to 4	9%	1,656
			Age 5 to 13	25%		Age 5 to 13	24%	
			Age 14 to 18	13%		Age 14 to 18	11%	
			Age 19 to 44	33%		Age 19 to 44	29%	
			Age ≥45	20%		Age ≥45	26%	
			Age not known	0%		Age not known	0%	
			Total	12,996		Total	3,953	
China	1,378,665,000	14,390	Age 0 to 4	3%	Data not available	Age 0 to 4	3%	Data not available
			Age 5 to 13	20%		Age 5 to 13	4%	
			Age 14 to 18	13%		Age 14 to 18	26%	
			Age 19 to 44	49%		Age 19 to 44	50%	
			Age ≥45	15%		Age ≥45	27%	
			Age not known	1%		Age not known	1%	
			Total	12,533		Total	1,857	
Brazil	207,652,865	12,119	Age 0 to 4	5%	3,556	Age 0 to 4	5%	0,578
			Age 5 to 13	16%		Age 5 to 13	15%	
			Age 14 to 18	11%		Age 14 to 18	13%	
			Age 19 to 44	49%		Age 19 to 44	47%	
			Age ≥45	18%		Age ≥45	19%	
			Age not known	0		Age not known	0	
			Total	10,123		Total	1,996	

Adapted from the data available on the Report on the Annual Global Survey 2016 (World Federation of Hemophilia, 2017). * The number of IU/capita is different in each region. The World Federation of Hemophilia has established that one international unit (IU) of FVIII clotting factor concentrate per capita should be the target minimum for countries wishing to achieve survival for the hemophilia population. Higher levels would be required to preserve joint function or achieve a quality of life equivalent to an individual without hemophilia. Only countries that completed the 2016 questionnaire were included in the report.



FIGURE 1

other responsibilities, helps the MoH to formulate public policies and develop technical guidelines.

Nevertheless, it is recognized that recently other NOGs and individuals have also pledged health rights through judicial institutions, such as the Public Chambers of Attorney and the *Brazilian Government Agency for Law Enforcement (in Brazil, Ministério Público)*.

Frequently, global care to PWH has been jeopardized by oscillations in CFC supply, exposing the patients to risks of bleeding and associated complications. The increased dismantling of the SUS and scrapping of public services, especially at state level, but also affecting the municipal and federal scope, is a challenge which can only be overcome through close cooperation with hemophilia patient societies and those that treat hemophilia. The infographic in Figure 1 presents a brief historical description of the achievements and obstacles of PWH in Brazil.^{8,9}

Brazil also has some unmet needs, such as the provision of faster and easier access to the most often necessary orthopedic surgeries and to hemophil-

ia laboratory diagnosis in some centers. A more organized health system should also educate the patients and their families so that they can take advantage of the treatment offered by the Haemophilia Centres (in Brazil, Hemocentros). Indeed, despite an appropriate prescription, 54% of patients do not understand and correctly adhere to the prophylaxis prescribed by healthcare practitioners.¹⁰

Although the benefits of prophylaxis are well established, this treatment is not available for all Brazilian PWH, and in many cases, it is not able to control the progression to hemophilic arthropathy. Considering the burden that chronic pain adds to the quality of life and daily life activities in PWH, the establishment of evidence-based guidelines for the evaluation and treatment of these complications is vital. When looking forward in healthcare provision, it is essential to prepare for the incorporation and application of new upcoming technologies, as well as to reduce the stigma associated with hemophilia in the general population, further educating patients, family members and non-specialist medical professionals about the disease.

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