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LETTER TO THE EDITOR

Regional registry of bleeding disorders in Tunisia

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Hereditary bleeding disorders have been reported worldwide. Haemophilia and von Willebrand's disease (VWD) are the most common disorders [1]. Other disorders are much rarer with high frequencies in countries where consanguineous marriages are frequent [2]. In developing countries there is limited information on bleeding disorders epidemiology. As there is no national registry for bleeding disorders in our country, it is difficult to ascertain how many patients have actually been diagnosed. In this study, we present for the first time the epidemiological data concerning bleeding disorders in Tunisia. The Hemophilia Treatment Center of Aziza Othmana Hospital (HTCAOH) has been working since 2002 independently of Clinical Hematology Department. A regional registry for our HTCAOH was set up since 2006. Patients are followed-up and every new diagnosed case is systematically registered.

Our HTCAOH has 320 patients who represent almost 60% of Tunisian patients with bleeding disorders. Among them 146 patients have haemophilia A and 33 patients have haemophilia B (86% were from the North regions of Tunisia (68% from N-E: Tunis, Nabeul, Bizerte and 18% N-W). Fifty-seven patients have VWD. The remaining 84 patients have rare bleeding disorders (Table 1).

The age distribution demonstrates that the most frequent category of age for haemophilia, VWD and other bleeding disorders is 19–44 years old, with frequencies of 43.18%, 36.48% and 50% respectively. Patients with haemophilia under 13 years old represent 38.54%, against 33.33% of patients with VWD and 10.71% of patients with other bleeding disorders (Fig. 1).

Patients with haemophilia are treated with plasma-derived products (81% of patients) and recombinant products, which have been introduced since 2008 (9% of patients included only haemophiliacs A). 35.4% of haemophiliacs A and 71% of haemophiliacs B have not been treated with cryoprecipitate, which we have stopped using since 2004 in our HTCAOH. Prophylactic treatment was used in 58 patients (27.62%) composed of 48 haemophiliacs A and 10 haemophiliacs B. The other pathologies are treated with the appropriate factor concentrate for each deficiency, PCC, FFP, platelet transfusions. We can also use the antifibrinolytic drugs for all bleeding disorders. No haemophiliac B developed inhibitors whereas nine haemophiliacs A developed inhibitors (seven patients with high responding inhibitors and two patients with low responding inhibitors).

Between December 2010 and December 2011 we have identified 20 haemophiliac new cases composed of 15 haemophiliacs A and five haemophiliacs B.

We initiated for the first time in our HTCAOH the molecular analysis of bleeding disorders since 2007. Seventy-five patients (Fig. 2) were screened for mutations responsible for their diseases [3–9].

According to the WFH global survey [10], Tunisia registered 200 patients with haemophilia in 2009. In our registry, we account 179 patients with haemophilia until December 2011, we can say that during the 2 years we improved diagnosis in our HTCAOH, but we must continue effort by education mainly since when we know that Tunisia (10 629 186 inhabitants in 2011) should include 706 potential patients with haemophilia according to the WFH guidelines and our HTCAOH which follows patients with haemophilia from North provinces (50% of Tunisian inhabitants) should include 353 patients which means 50% of haemophiliacs may not be identified. In the same time, the low life expectancy in our country compared to other countries may explain the lower number of haemophiliacs than expected.

On the basis of the comparison with countries having a similar population number reported in WFH Global Survey 2009, we found similar distribution for haemophilia, which is the most frequent in our country and also in our registry as many other reported countries (Table 2), since haemophilia represents the most common type of hereditary factor deficiencies reported around the world concerning identified patients [1].

Relative to haemophilia B, haemophilia A occurs with a frequency of 81%, which is nearly as the reported frequencies 80% to 85% [1]. The severity frequencies (51% severe, 33% moderate and 16% mild) show a similar distribution with other reported data in whom the severity form is the most frequent, followed by moderate and mild forms [1].

Exactly 38.54% of our patients with haemophilia are relatively of young age, under 13 years. Compared with Belgium and Portugal

Table 1. Distribution of bleeding disorders in HTCAOH.

Deficiency disorder	Number of patients	Number of women
Haemophilia A	146	0
Severe	75	
Moderate	49	
Mild	22	
Haemophilia B	33	1
Severe	18	
Moderate	9	
Mild	6	
von Willebrand's disease	57	35
Type 1	12	
Type 2	16	
Type 3	23	
Unknown	6	
Rare bleeding disorders	84	45
Glanzmann's thrombasthenia	23	
Factor I deficiency	17	
Factor V deficiency	5	
Factor VII deficiency	12	
Factor V+VIII deficiency	5	
Factor X deficiency	2	
Factor XI deficiency	2	
Factor XI+VIII deficiency	3	
Factor XIII deficiency	2	
Bernard-Soulier	3	
Unknown disorders	9	

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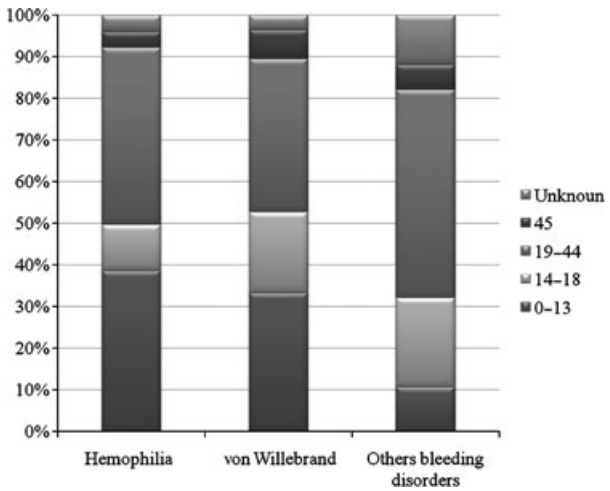

Fig. 1. Age distribution of HTCAOH patients.

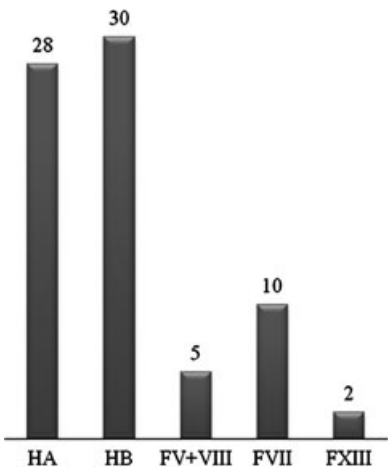

Fig. 2. Number of patients in whom genetic analysis of mutations was performed.

Table 2. Comparison of bleeding disorders distribution with countries having a similar number of population.

	HTCAOH 2011	Tunisia 2009*	Belgium 2009*	Portugal 2009*
Population	5 181 500	10 486 339	10 423 493	10 735 765
Number of PWHA	143	162	874	506
Number of PWHB	33	38	196	151
Number of patients with VWD	57	76	1193	51
Number of patients with OBD	87	112	390	14

*Data are from WFH global survey 2009.PWHA, patients with HA; PWHB, patients with HB; OBD, other bleeding disorders.

which have respectively 17.94% and 13.14% of haemophiliacs under 13 years (Table 2), we can say that we make a progress in the precocity of diagnosis (half the number of patients are diagnosed before the age of 2 years).

Frequency of inhibitors in our patients with haemophilia (6%) is lower than that reported in other cohorts [10]. Since the development risk is multifactorial, our data are still incomplete to explain the lower frequencies.

Concerning VWD, we found that the reported number of patients (57) is lesser than that expected in Tunisia (1% in general population). The type 3 is the most frequent (41%) followed by type 2 (28%) and type 1 (21%). This reversed distribution is mostly observed in developing countries and it may be due to the easier diagnostic of severe form than the type 1, which is an asymptomatic form.

We are more advanced than Egypt and we are in the same situation with Portugal, but it is better diagnosed in Belgium so we need to make more efforts to identify patients with this pathology. We cannot be compared with Algeria, Morocco and Libya since no data were reported in WFH global survey 2009 (Table 3).

Other bleeding disorders represent 26% of all bleeding disorders (Table 4). It is not the case in other reported data [10]. Based on WFH data, the situation is similar in Egypt and we can explain this with the high frequency of consanguineous marriage or by under diagnosis of the less severe forms of VWD. In Belgium and Portugal it is not the same case since other bleeding disorders are less frequent. In our registry, the most frequent disorders are, respectively, Glanzmann, FID and FVIID. In Egypt, it is the same case for Glanzmann, which is the most frequent disorder, but it is followed by FXD and FID. The most frequent disorder in Belgium is FXID followed by FVIID, Glanzmann and FVD. For Portugal, we found in the first position FXID, followed by FVD. This different distribution in bleeding disorders in the four countries can be explained by the difference in ethnic groups. In addition, we mention that we have all types of bleeding disorders even the rarest disorders such as FV + VIIID and FVIII + XID. The last one may be not identified in Belgium and Portugal. The unique bleeding disorder, which is absent in our HTCAOH and not reported in Belgium and Portugal is FIID.

For the total number of other bleeding disorders we found that despite our small population against the Egyptian one (80, 471, 869), we can say that they are better diagnosed in our HTCAOH since we have 84 against 60 patients with other bleeding disorders from Egypt according to the WFH global survey, 2009. We cannot make a comparison with the three other neighbouring countries (Algeria, Morocco and Libya), which are similar to us in development degree because of lack of information concerning these disorders.

Since 50% of patients with autosomal bleeding disorders are women, the HTCAOH staff provide the best care during pregnancy and childbirth to minimize the possible complications for both mother and the newborn. In addition, they receive genetic counselling about the risks of having a child with this deficiency.

In conclusion, we reported in this article for the first time in Tunisia a regional registry for patients with inherited bleeding disorders initiated in 2006. In future, we will focus to continue data entries which will enable us to increase our knowledge on the prevalence of these disorders in our country to improve the support of our patients, to anticipate the needs, to provide information concerning the characteristic of bleeding disorders, to complete molecular characterization of the genetic mutations and to follow correlation with the phenotype in our patients. At the same time, we plan to collaborate with the HTC of the Centre and South Tunisia to develop it at a national level to create more awareness among the medical staff

Table 3. Comparison of age distribution.

	HTCAOH	Belgium	Portugal
Total of patients	179	1070	657
0–13 years old	69	183	75
Frequency	38.54%	17.94%	13.14%

Table 4. Distribution of bleeding disorders in HTCAOH and other countries.

Country	VWD	FID	FIID	FVD	FV+VIIID	FVIID	FXD	FXID	FVIII+XID	FXIIID	Platelet dis. Glanz	Platelet Dis. Bernard. S	Platelet Dis. unknown
HTCAOH	57	17	0	3	5	12	2	5	3	2	23	3	8
Egypt	25	8	1	4	1	4	12	1		4	20		
Belgium	1193			16		46	4	72		2	17		
Portugal	51	2		3			1	7		1	1		6

No data are available for the empty boxes.
VWD, von Willebrand's disease; FID, factor I deficiency; FIID, factor II deficiency; FVD, factor V deficiency; FV+FVIIID, factors V+VIII deficiency; FVIID, factor VII deficiency; FXD, factor X deficiency; FXID, factor XI deficiency; FVIII+FXID, factors VIII+XI deficiency; FXIIID, factor XIII deficiency; Platelet dis., platelet disorders; Glanz, Glanzmann's thrombasthenia; Bernad. S, Bernard Soulier.

and society, on the existence of this affliction and the need to organize their support in countries with limited resources like our country.

Author contributions

EH performed the research analysed the data and wrote the paper; CA, BLF and BW analysed the data; ZK and ZM contributed in the data collection; MB and GE designed the research.

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Disclosures

The authors stated that they had no interests which might be perceived as posing a conflict or bias.

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