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LETTER TO THE EDITOR

Inherited coagulation disorders in the northwestern region of Iran

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According to the global survey carried out by World Federation of Haemophilia, Iran with 3463 haemophilic patients was ranked as the second in the eastern Mediterranean region next to the Egypt having 4141 cases of haemophilia. Of this 58 patients are human immunodeficiency virus (HIV) positive and 3198 are infected with hepatitis C virus. The prevalence rate of disease was estimated to be about 5.4 per 100 000 people [1]. The aim of this study was to document the epidemiological features, disease severity and complications associated with inherited coagulation disorders as focused in the northwestern region of Iran.

Medical history of all cases (174 persons) diagnosed with inherited coagulation disorders were studied in Haematology–Oncology Department, Tabriz University of Medical Sciences between 1994 and 2004. This department is the unique adult centre in East Azerbaijan (the northwestern part of the country) providing clinical services for adult haemophilic patients. All subjects were diagnosed based on the criteria of the Iranian Registry of Coagulation Disorders and confirmed with haemophilia, von Willebrand disease (VWD) or other coagulation factors deficiency. Disorders were classified as mild, moderate or severe according to the level of plasma clotting factor: 5–25%, 1–5% and <1% respectively [2]. Data collected includes age, clinical characteristics, resident status and type of disorders. Standard enzyme immunoassays were applied for the diagnosis of hepatitis B virus, hepatitis C virus (HCV) and HIV. Rates of prevalence, 95% confidence interval (CI) and descriptive statistics were calculated to document the epidemiological features of the disorders in the region. Total population by age groups was obtained from the Demographic Centre for the East Azerbaijan, and used as denominator in computing prevalence rates.

The basic characteristics for the subjects of the study are presented in Table 1. The age of the patients in all groups of disorders ranged between 10 and 66 years as averaged 26.7 with standard deviation of 10. Nearly half of the subjects were located in Tabriz, one of the major cities of Iran, which represents the proportionally normal distribution of the study sample in the population of the region. No female haemophilic patient was identified among the subjects within the 10 years of study from 1994 to 2004.

The majority of the subjects (69%) suffered from haemophilia A, followed by 11% haemophilia B and 10% VWD. Other types of disorders were included in the remaining 10%. Table 2 shows the prevalence of inherited coagulation disorders by age groups.

Total prevalence of disorders was estimated 5.7 per 100 000 populations (95% CI: 4.8–6.5) in the area. The highest prevalence of disorders was shown to fall in 20–29 years of age group (9.6 per 100 000 people, 95% CI: 7.6–12.0) while the lowest rate was observed among those with 40–49 years of age (2.7 per 100 000 people, 95% CI: 1.4–4.9). The prevalence rate of disorders in those with more than 49 years of age was 2.8 per 100 000 people (95% CI: 1.7–4.5) as described in Table 2. Correlation between age group and the prevalence of inherited coagulation disorders was shown to be significant.

Table 3 describes the infectious status of patients. As of this data, only two patients were tested positive for Hbs-Ag when compared with 74 who were negative among haemophilia A patients. Meanwhile, 41% was infected with HCV. Eight haemophilia B subjects (44%) were Hbs-Ag negative, and seven cases (39%) had positive result of HCV. A total of

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Table 1. Basic characteristics and frequency distribution of inherited coagulation disorders.

Type	Mean age (SD)	Median	Range
Haemophilia A	26.7 (10)	24.0	11–65
Haemophilia B	23.4 (7.3)	23.5	10–36
Von Willebrand disease	25.8 (7.6)	24.0	16–43
Others*	32.1 (13.3)	29.0	16–66
Total	26.7 (10)	24	10–66
Type of disorder	**Frequency**		**Per cent**
Haemophilia A	120		69.0
Haemophilia B	18		10.3
Von Willebrand disease	18		10.3
Factor 7	2		1.1
Factor 10	2		1.1
Factor 13	4		2.3
Platelet disorder	7		4.0
Factors 5 and 8	2		1.1
Factors 2, 7 and 9	1		0.5
Residence status			
Tabriz	73		41.7
Other cities	101		58.3

*The others include factors 7, 10, 13, 5 and 8, 2 and 7 and 9 and platelet disorder.

Table 2. Prevalence of inherited coagulation disorders by age groups in the northwestern region of Iran.

Age groups	Frequency	Per cent	Population	Prevalence (per 100 000)	Confidence interval (95%)
10–19	35	20.1	697 945	5.01	3.4–6.9
20–29	78	44.8	808 423	9.6	7.6–12.0
30–39	32	18.4	547 493	5.8	3.9–8.3
40–49	11	6.3	399 702	2.7	1.4–4.9
50+	18	10.4	632 446	2.8	1.7–4.5
Total	174	100	3 086 009	5.7	4.8–6.5

54% of HCV infection was associated with severe haemophilia, while 26% and 14% with moderate and mild haemophilia respectively. Families with more than one haemophilic patient were as much as 47 (34%). Only one patient was tested positive to anti-HIV who died 6 years ago. In our hospital, the mean quantities of factor VIII for severe, moderate and mild haemophilia A patients were shown to be 49, 22 and 8.1 × 500 IU per year respectively. While mean quantities for cryoprecipitate were 61, 36.5 and 33 bags per year.

In Iran, haemophilia A is usually treated with a wider spectrum of products including single-donor cryoprecipitate and factor VIII concentrates [3]. On the contrary, because of the limitation in financial resources, cryoprecipitate or fresh frozen plasma is sometimes used repeatedly together with purified factor VIII. Therefore, the prevalence of patient contamination to virus infections was expected to be high in the region. The majority of our patients were treated with cryoprecipitate. Factor VIII concentrate was administered when available. The treatment and follow-up of youngsters were performed in paediatric hospital, so we have no data regarding initiation, duration and frequency of their exposure to blood products. This is a major obstacle in this study.

Hepatitis C is a major health problem with the average prevalence of 3% ranged between 0.1% and 5% in various countries. No HCV transmission has been reported since 1986 in countries having access to viral-inactivated concentrates. However, it still poses a major problem in countries where single donor unsterilized concentrate is used [4]. In Shiraz, a major city in southern Iran, hepatitis B antigen (HBs-Ag), anti-HCV and anti-HIV were reported as positive in 0.7%, 16% and 0.4% of haemophilic patients respectively [5]. Despite having access to known number of patients tested positive for HBs-Ag and HCV antibody (HCV-Ab), it was impossible to determine the rate of infection and its correlation to severity of the disease because of necessity to test all patients.

In Gilan, a northern province of Iran, 27% and 72% of haemophilic patients were tested positive for HBs-Ag and HCV-Ab respectively. Seropositivity for HCV-Ab correlated with the duration of treatment with clotting factor [6]. They also found that the prevalence of HBs-Ag positive cases in Gilan province was higher compared with other areas in the country [6]. Despite of inability to determine the infectious status of many cases of haemophilia A and B through their recording profiles, we could estimate that our HCV positive cases were fewer than those reported from the Gilan. Our data are similar to

Table 3. Infectious status of haemophilia A and B patients.

	Total	HBs+	HBs−	Unknown	HCV+	HCV−	Unknown
Haemophilia A	120	2	74	44	50	23	47
Haemophilia B	18	0	8	10	7	1	10

HBs+, hepatitis B antigen positive; HBs−, hepatitis B antigen negative; HCV+, hepatitis C antibody positive; HCV−, hepatitis C antibody negative.

those reports from India (Ghosh *et al.*) [7], Brazil (Succi *et al.*) [8] and Turkey (Kocabas *et al.*) [9].

This study showed lower occurrence of HBs-Ag positive cases compared with the similar reports from neighbouring countries. This may reflect the appropriate vaccination against this virus in Iran in recent years. Although vaccination is not available against HCV but we could suggest using sterilized products to reduce the rate of virus transmission.

It is concluded that in Iran, like some other Muslim countries where consanguineous marriages are still common in rural areas, deficiencies in clotting factor are observed frequently [10]. This indicates that preconception educational programmes should be conducted for young couples to prevent inherited coagulation disorders.

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