Hemophilia A in Afghanistan, the first report

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Hemophilia A is the most severe congenital bleeding disorder with estimated incidence of 1 per 5000 live male birth. Afghanistan located within south Asia and central Asia have a considerable number of patients with bleeding disorders that is accompanied by low government resources and limited diagnostic facilities. This study aimed to evaluate different aspects of hemophilia A in Afghanistan for the first time. This study was conducted on 167 patients with hemophilia A who were referred to hemophilia center of Kabul city. The diagnosis of the disease was performed based on standard questionnaire, evaluation of clinical manifestations and family history as well as laboratory assays. Diagnose of hemophilia A was confirmed by coagulation factor VIII (C: FVIII) assay. The mean age and mean age at diagnosis were 13.7 ± 2.4 and 1.4 ± 0.7 years, respectively. The mean FVIII level was 0.7 IU/dl. The most common clinical manifestation was hemarthrosis, which was detected in 80% of patients. According to geographical distribution, 42% of patients are residents of Kabul Province. About 41% of patients were Tajik, whereas 37% were Pashtun. In Afghanistan, as a country with low number of diagnosed patients with hemophilia A because of limited diagnostic and treatment facilities, high amount of investments are required in order to improve the quality and quantity of hemophilic patients. *Blood Coagul Fibrinolysis* **30:000–000**

Blood Coagulation and Fibrinolysis 2019, **30**:00–00

Keywords: Afghanistan, clinical manifestations, diagnosis, hemophilia A

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Received 10 September 2018 **Revised** 10 July 2019
Accepted 21 August 2019

Introduction

Hemophilia A is an X-linked recessive bleeding disorder, which results from different kinds of mutations in *F8* gene [1]. The estimated prevalence of hemophilia A as the most common severe inherited bleeding disorders, is 1 in 5000 male live births [2–4]. The disorder presents with a wide range of clinical features, including ecchymosis, epistaxis, posttrauma bleeding, gastrointestinal bleeding, hemarthrosis, hematoma and central nervous system (CNS) bleeding. The severity of the disorder is directly related to residual factor VIII (FVIII) coagulant activity (FVIII:C) [3,5]. The most common symptoms of hemophilia A are joint and muscle bleedings, which usually occur when the child starts to walk [6]. However intracranial hemorrhage (ICH) is the main cause of death in patients with haemophilia, which accounted for 20% of mortalities [7,8]. On the basis of factor activity, hemophilia A is divided into three groups, mild (>5 to 30%), moderate (1–5%) and severe (<1%) [2]. Afghanistan located within south Asia and central Asia with high rate of consanguineous marriage has a great number of patients with different kind of inherited bleeding disorders. This high frequency is accompanied with limited government resources, restricted diagnostic facilities and public awareness [9]. Unfortunately, few studies were performed on these disorders. Therefore, in this study for the first time, we aimed to evaluate different characteristics of hemophilia A patients including demographic data, prevalence, clinical manifestations, distribution and ethnicity in this country.

Method

Data collection

This descriptive study is conducted on patients suspected to hemophilia A who were referred to hemophilia center of Kabul city. Data was collected by laboratory assessments as well as a standard questionnaire including age, sex, self-reported ethnicity, age of diagnosis, clinical manifestations, parental consanguinity and family history of death, and so forth. All patients or their parents (in the cases under 18 years old) were interviewed by an expert staff to fill the questionnaire. The study is approved by local ethical committee and the informed consent was obtained from all participants.

Screening and diagnosis of patients with hemophilia A

The diagnosis of the disorder is performed based on clinical presentations, family history and laboratory assays. Initially all patients were physically examined by an expert physician. Then suspected individuals were referred to clinical laboratory for assessment by routine coagulation laboratory tests including prothrombin time (PT), partial thromboplastin time (aPTT), thrombin time (TT), bleeding time and platelet count. Patients with prolonged aPTT, but normal PT and bleeding time were

 DOI:10.1097/MBC.0000000000000853

evaluated by factor activity assay in order to confirm hemophilia A. Plasma FVIII activity was measured by one-stage FVIII assay. Severity of disease was classified based on the FVIII activity level, as severe (<1%), moderate (1–5%) and mild (>5–30%). In order to rule out FVIII inhibitors, the mixing study was performed with Bethesda assay method as described previously. Due to lack of factor assay in Afghanistan, FVIII activity and inhibitor assays were performed in Iran[10,11].

Results

Demographic and laboratory results

During the period of the study, 167 patients with hemophilia A were diagnosed. The mean age at diagnosis was 1.4 ± 0.7 years old, and the minimum and the maximum age of diagnosis were at the birth and 9 years old, respectively. Among 110 patients with available data of family history, the majority (79%) had positive family history and 42% had at least one history of death because of hemophilia A. Parental consanguinity was observed in about 60% of the patients. Almost 55% of the patients had severe hemophilia A, whereas 40.9% and 3.6% had moderate and mild hemophilia A, respectively. The mean of FVIII level was 0.7% (0.4–13%) (Table 1).

Clinical manifestations

The most common clinical features, which lead to diagnosis of hemophilia A were hemarthrosis and epistaxis, which occurred in ~80 and ~66% of the patients, respectively. Sixty percent of the patients, with hemarthrosis, had severe hemophilia A, whereas 30.7% had moderate hemophilia A. Among all patients, 44% experienced hematoma that 68.5% of them had severe hemophilia A, and 29% were affected by moderate type of the disease. Gum bleeding was the les common clinical presentation, was observed in ~11% of the individuals. Other types of bleeding episodes are ecchymosis, easy bruising and swelling, postdental extraction bleeding and hematuria. Moreover, 7 (4.1%) patients had a history of internal bleeding. There is a 10-year-old boy with mild hemophilia A and mental retardation (Table 2).

Geographical distribution and ethnicity

The majority of the patients were residents in Kabul Province (42%), followed by its neighboring province, Parwan (12%). The other provinces had low number of patients (Fig. 1).

On the basis of ethnicity, the majority of patients were Tajik (41%) and Pashtun (37%). The other ethnicities including Sadat and Uzbek accounted for 5% of the patients. No patient with the Baluch ethnicity was diagnosed (Fig. 2).

Discussion

Hemophilia A is the most severe congenital bleeding disorder with a high rate of morbidity and mortality. According to the 2016 annual report of the World Federation of Hemophilia (WFH), Afghanistan with 289 patients with hemophilia A had a high number of these patients. In our study, a total of 167 patients with hemophilia A were diagnosed that in comparison with neighboring country, Iran with 5008 patients with hemophilia A, this number is very low. In fact, this low number of patients is due to low diagnostic facilities in this country and a low economical ability of people. The number of laboratories with coagulation-specific tests is low and most of people had to travel to Kabul city. In addition, few hematologist and even internal medicine physicians are available in Afghanistan; most of them are working in big cities, such as Kabul, Herat and Kandahar. In this study, about two-third of the patients with hemophilia A were residents in Kabul and adjunct cities, such as Wardak and Parwan provinces. A glance to Afghanistan map shows that almost no patients with hemophilia A was diagnosed in Nimroz, Helmand and Kandahar as well as Farah and Zabul provinces with high distance from

Table 1 The demographic information of patients with hemophilia A

	Number (%)	Mean age at diagnosis (years)	Family history, *N* (%)	History of death, *N* (%)	Parental consanguinity, *N* (%)	Mean factor level
All patients	167	1.4	87 (79)[a]	46 (41.8)[a]	80 (59.7)[b]	0.7
Severe	92 (55.4%)	1.3	50 (54)	26 (28.2)	38 (41.3)	0.7
Moderate	69 (40.9%)	1.6	38 (55.8)	20 (29.4)	39 (57.3)	1.8
Mild	6 (3.6%)	4.7	1 (16.6)	1 (16.6)	2 (33)	9.8

N, number. [a]Data of 57 cases were not available. [b]Data of 33 cases were not available.

Table 2 Clinical manifestations of patients with hemophilia A

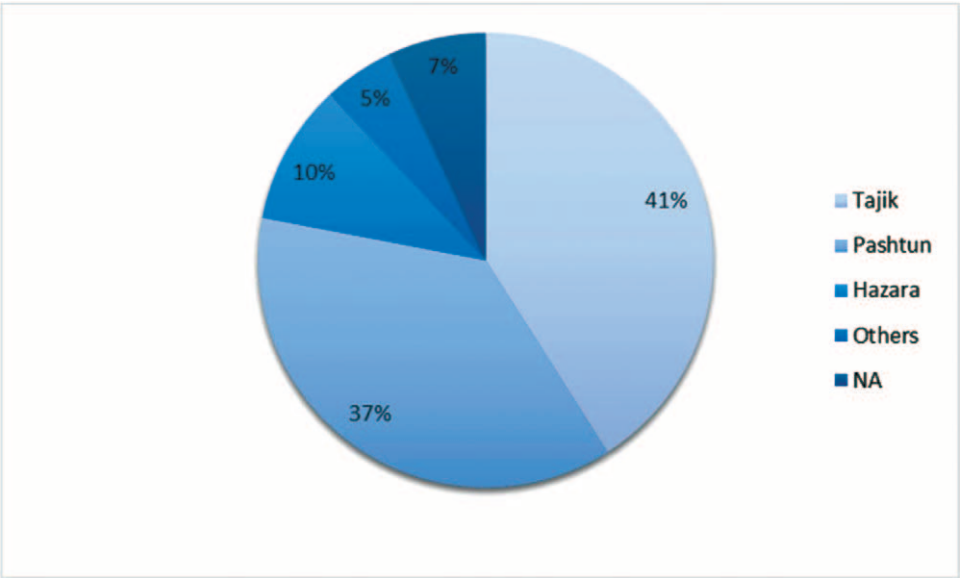
	Total number	Epistaxis, *N* (%)	Gum bleeding, *N* (%)	Hemarthrosis, *N* (%)	Hematoma, *N* (%)	Postdental extraction bleeding, *N* (%)	Easy bruising, *N* (%)	Hematuria, *N* (%)	Ecchymosis, *N* (%)	GI bleeding
All patients	167	111 (66.4)	18 (10.7%)	135 (80.8)	73 (43.7)	48 (28.7)	46 (27.5)	40 (24.5)	48 (28.7)	36 (21.5)
Severe	92	56 (60.8)	6 (6.5)	81 (88)	50 (54.3)	20 (21.7)	17 (18.4)	27 (29.3)	34 (36.9)	25 (27.1)
Moderate	69	49 (71)	10 (14.7)	50 (73)	21 (30.8)	9 (13.2)	28 (41.1)	12 (17.6)	13 (19.1)	10 (14.7)
Mild	6	5 (83.3)	2 (33)	4 (66)	2 (33)	2 (33)	–	1 (16.6)	1 (16.6)	1 (16.6)

GI, gastrointestinal; *N*, number.

Fig. 1

Distribution of hemophilia A in Afghanistan.

Fig. 2



Ethnicity distribution of patients with hemophilia A in Afghanistan. Na, not available.

Kabul. This issue shows that almost all diagnostic facilities were concentrated in Kabul City and most of other cities had very restricted diagnostic and therapeutic facilities. This situation even in comparison with neighboring countries is catastrophic and high investment in these areas of Afghanistan is required. It seems that a limited resource is the main reason for low number of diagnosed patients with hemophilia A in the country. In other hand, the number of deaths is high in affected families and about half of patients with hemophilia A had a positive history of hemophilia A related death. This number is high in comparison with Iran, Pakistan and most other countries. The main reason for this high number of deaths among these patients is late diagnosis of the disorders that is because of few number of governmental and almost lack of private laboratories in most of the provinces. Among patients with hemophilia A in the country, about two-third had severe form of disorder that is in agreement with other studies [12,13]. These patients had higher rate of severe clinical presentations, such as gastrointestinal bleeding, hemarthrosis and hematoma that is in agreement with other studies [13,12]. As patients with severe hemophilia A had severe presentations and required more medical interventions, the number of patients with this form of disorder is higher in our study. In our study, nobody had CNS bleeding that is not in agreement with other similar studies, even in neighboring countries [12,14,15]. It seems that because of low medical facilities, most of patients with CNS bleeding die and this is one the main reasons for high rate of mortality in patients with hemophilia A in Afghanistan. In conclusion, in a country such as Afghanistan with low number of diagnosed patients with hemophilia A and high rate of mortality as well as limited diagnostic and treatment facilities, high amount of investments that significantly can improve the quality and quantity of treatment by governmental and privates resources are required.

Acknowledgements

The financial support of Kateb Medical Research Center is appreciated.

Conflicts of interest

There are no conflicts of interest.

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