Original Article

Pattern of Common Inherited Coagulation Disorders: Evaluation of 100 Cases

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Abstract

Introduction: The bleeding disorders having inherited abnormality of haemostasis may present with significant difficulties in diagnosis and management. The overall frequency of these disorders in the general population is low.

Objectives: To study the frequency of inherited coagulation disorders and their prevalent clinical manifestations.

Materials and Methods: A prospective cross sectional study of one hundred patients of all age group and both sexes was organized as both in-patient and out-patient based in the Department of haematology, Armed Forces Institute of Pathology (AFIP) from July 2012 to June 2013.

Results: In this study, out of 100 patients, haemophilia A, diagnosed in 75% patients, was the most common disorder. Age group ranging from 5-15 years constituted 48% of total patients. Male to female ratio of patients having hereditary coagulation defect was 73:2 in haemophilia A whereas 2:3 in vWD. Consanguinity was documented in 60% of vWD and 24% of haemophilia A. The most common clinical symptom in hereditary coagulation defect (HCD) was echymosis (60%). The most common presenting feature of haemophilia was haematoma (57.95%) whereas menorrhagia was the most common presentation of female patients with vWD. Among 97 patients of haemophilia and vWD, 59(60.82%) cases were in mild form and 04(4.12%) cases were found to have severe coagulation defect. Fresh frozen plasma (FFP) is the most common modality of treatment in HCD.

Conclusion: It has become the need of the time to find out such a cost effective diagnostic parameter to make an early diagnosis of inherited coagulation disorders.

Key-Words: Hereditary coagulation defect, Von Willebrand disease, Rare inherited coagulation disorder.

Introduction

The existence of lifelong bleeding disorders and their familial occurrence was noted very early in the medical literature by Alsaharavius during tenth century[1]. According to the World Federation of Haemophilia (WFH), the general term 'bleeding disorders' defines a broad range of medical problems that lead to poor blood clotting and thus continuous or uncontrollable bleeding. Bleeding disorders can be classified as acquired or inherited, and as affecting primary or secondary haemostasis[2]. Hereditary disorders of coagulation usually are the results of a deficiency or abnormality of a single plasma protein. Though, hereditary coagulation disorders are rare[3].

Haemophilia A and B are the most frequent inherited X-linkedbleeding disorders include 95% to 97% of all the inherited deficiencies of coagulation factors. VWD is a relatively common cause of bleeding, affecting 1-3% of the population worldwide[4]. The remaining defects, generally transmitted as autosomal recessive traits in both sexes, are rare, with prevalence of the presumably homozygous forms in the general population ranging from approximately one per million for factor V, one in 2 million for factor II and factor XIII deficiency to one in 500000 for factor VII (FVII) deficiency. Consequently, diagnosis and monitoring of affected individuals may require specialized phenotypic and molecular investigations that are not widely available[5,6].

Materials and Methods

A prospective type of cross sectional study among 100 cases was conducted in the department of Haematology, Armed Forces Institute of Pathology (AFIP), Dhaka Cantonment, Dhaka from July 2012 to June 2013. Patients of all age group and both sexes attending with a history of bleeding manifestations for coagulation factor assay were included as convenient sampling. Patients who had given consent, established cases with bleeding manifestations, having positive family history and prolonged APTT were included in this study. Patients who were on anticoagulant drugs, having known medical diseases leads to bleeding diathesis, and patients who were advised for bone marrow examination for the diagnosis were excluded from this study. Written informed consent was obtained from the patient or legal guardian for this study. Patient confidentiality was strictly maintained.

Results

Out of 100 patients; 90% was male, 10% female, mean age of total patients was 9.45±7.58 years and 48% was in age group 5-15 years. Among total patients; haemophilia A was the most common disorder (75%) followed by haemophilia B (12%), vWD (10%), RICD (2%) and fibrinogen deficiency in 1%. The most common clinical symptom in HCD was echymosis (60%) and most frequent presenting feature of haemophilia was haematoma (51%) whereas most of patients with vWD presented with mucocutaneous bleeding. Menorrhagia was the most common

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presentation of female patients with vWD. Although few study patients presented with multiple types of bleeding (Table-I). Positive family history was detected in 70% of vWD, 68% of haemophilia A, 50% of haemophilia B and 50% of cases with RICD. Consanguinity was documented in 60% of vWD, 24% of haemophiliaA, 16.67% of haemophilia B, 100% of fibrinogen deficiency and 50% of cases with RICD (Table-II).

Almost all the patients had prolonged APTT except 1 patient of RICD. PT was found normal in almost all cases except 1 patient with fibrinogen deficiency and 1 patient of RICD. In case of vWD, 2 patients had prolonged BT. CT was prolonged only in 4 severe haemophilia cases. One patient of RICD had normal spectrum of coagulation profilebut the urea clot solubility test was positive (Table-III). Out of 100 cases, 13 were treated by whole fresh blood, 50 were given FFP, 15 were replaced by specific factor, Tranexamic acid were taken by 10 and 2 were treated by herbal method whereas 10 cases were found without any treatment. It was obvious that FFP is the most common modality of treatment in HCD (Table-IV).

Table-I: Distribution of patients by age, sex, types of bleeding and diagnosis (n=100)

Characteristics		Total patients	Haemophilia		vWD	Fibrinogen deficiency	RICD
			A	B			
Age (year)	0-5	31	21	04	05	00	01
	5-15	48	39	05	03	01	00
	15-25	15	10	02	02	00	01
	>25	06	05	01	00	00	00
	Total	100	75	12	10	1	2
	Mean±SD	9.45±7.58	9.52±7.20	8.50±8.22	8.70±7.42	6.0±0.0	10.0±7.07
Sex	Male	90	73	12	4	0	1
	Female	10	2	0	6	1	1
Types of bleeding	Echymosis/Bruising	40	08	10	01	01	-
	Epistaxis	05	-	06	-	-	-
	After circumcision	18	02	01	-	-	-
	After dental procedure	29	04	08	-	01	-
	Gum bleeding	10	01	05	-	01	-
	After trauma	30	08	06	01	-	-
	Haematoma	45	06	05	-	01	-
	Joint bleeding	31	05	-	01	-	-
	Menorrhagia	01	-	03	-	-	-
	Haematuria	-	01	-	-	-	-
	Umbilical cord bleeding	03	-	-	-	-	-

Table-II: Distribution of patients by family history, consanguinity and diagnosis (n=100)

Types of disorders	Total Patients	Positive history	
		Family history n(%)	Consanguinity n(%)
Haemophilia A	75	51(68)	18(24)
Haemophilia B	12	6(50)	02(16.7)
vWD	10	7(70)	06(60)
Fibrinogen deficiency	1	–	01(100)
RICD	2	01(50)	01(50)

Table-III: Distribution of patients by spectrum of coagulation profile (n=100)

Disorder	BT	CT	PT	APTT	Factor assay
Haemophilia A	Normal	Prolonged (3) Normal (72)	Normal	Prolonged	Factor VIII reduced
Haemophilia B	Normal	Prolonged (1) Normal (11)	Normal	Prolonged	Prolonged
vWD	Normal (8) Prolonged (2)	Normal	Normal	Prolonged	vWF : Ag reduced
Fibrinogen deficiency	Normal	Normal	Prolonged	Prolonged	Factor 1 reduced
RICD	Normal	Normal	Prolonged(1) Normal (1)	Prolonged (1) Normal (1)	Factor VIII, IX, vWF: Ag and mixing test-normal.

Table-IV: Distribution of patients by treatment received (n=100)

Modality of treatment	Haemophilia		vWD	Fibrinogen deficiency	RICD
	A	B			
Fresh whole blood	10	02	01	-	-
Fresh frozen plasma (FFP)	38	06	04	01	01
Factor replacement	13	02	-	-	-
Tranexamic acid	06	01	03	-	00
Herbal treatment	02	-	-	-	-
No treatment received yet	06	01	02	-	01

Discussion

Out of 100 study cases, haemophilia A, diagnosed in 75% patients, was the most common disorder followed by haemophilia B in 12%, vWD in 10% and fibrinogen deficiency in 1% case while the rare inherited coagulation disorders (RICD) in 2% cases. That result was compared with Karimiet al[7] study showing overall 411 patients had common bleeding disorders including 326 haemophilia A, 46 haemophilia B, and 39 von Willebranddisease. In another study, Zaidi et al[8] reported among fifty cases, the commonest hereditary coagulation disorder was haemophilia (30%), followed by von Willebrand disease (26%) and Christmas disease (14%). The rare autosomal recessive hereditary coagulation disorders together constituted 30%. This result showed approximately similar to this study. Regarding the age distribution of the study patients, 5-15 years age group constituted 48% in total patients. That result was compared with Borhany et al[9] study in which mean age (in years) in Haemophilia A 15.8, in Haemophilia B 15.6, in vWD 17.3 and in RICD 13.2, that is dissimilar to this study. The cause of late presentation in this study is that he mainly dealt with the bleeding disorder in adults. But Gupta et al[10] found patients with inherited coagulation disorders had variable age of onset of bleeding manifestation (birth to 35 years) with a mean of 7.2 years which is similar to this study. In other study Emanet al[11] found mean age was 7.84(±3.44) that is also similar to this study.

Regarding sex distribution, as haemophilia is X-linked hereditary disorder, the cases were seen mostly in males with the exception of 2 female cases in haemophilia A whereas M:F in haemophilia B, vWD, fibrinogen deficiency and RICD were 12:0,2:3, 0:1 and 1:1 respectively. That result was compared with Zaidi et al[8]. They found male to female ratio (M:F) inhaemophilia A were 15:0, haemophilia B were 7:1, vWD 1:1 and fibrinogen deficiency 2:1. In this study exception of 2 female cases in haemophilia A that is similar to

Borhany et al[9] study reporting 5 haemophilia carriers with positive family history of bleeding in first- degree relatives. In another study Gupta et al[10] M:F ratio 456:3, haemophilia (A, B), vWD 42:40 and fibrinogen deficiency 3:2, RICD 8:5 which is almost similar to this study. Regarding the percentage of patients with positive family history and consanguinity, the result is similar to findings of Emanet al[11]. A positive family history was reported in 83.3% (10 out of 12) of VWD children. Consanguinity was found in 66.7% (8 out of 12) of vWD cases (but doubt remains if it is commoner in type 3, as they studied four cases with type 3, each two cases were members of one family). Gupta et al[10] found family history of bleeding manifestations was present in 17.8% of patients with haemophilia and 21.9% of patients with vWD. Zaidi et al[8] study showed positive consanguinity in 40% of haemophilia A, 69% of vWD and 43% of haemophilia B that is approximately similar to this study. The reason for increased percentage of positive family history in this study was more number of referral cases in this study samples.

Our seriesexpressed the clinical manifestation of 100 patients. Borhanyet al[9] had shown, the most common type of bleeding was haemarthrosis (43.35%) in HaemophiliaA and Haemophilia B; followed by haematoma (37.7%), gum bleeding (13.5%), haematuria (11.6%), easy bruising (9.1%), menorrhagia (6.6%), intracranialhaemorrhage (ICH) (5.0%), epistaxis (3.7%). In other study by Eman et al[11] epistaxis was documented in 63.3% (7 out of 11) of haemophilia A cases, 33.3% (1 in3) of haemophilia B cases. Gupta et al[10] study also found the most common presenting feature of haemophilia was haemarthrosis (77.7%) whereas most of the patients of vWD (67%) presented with mucocutaneous bleeding. These findings are almost nearer to this study. The reason for the difference of haemarthrosis with my study is that, they had carried out a hospital in-patient based cross-sectional study as a whole. This study showed the distribution of haemophilia and vWD according to severity. It was documented that mild form was more common whereas no severe form was found in case of vWD. These findings are almost nearer to study of Zaidi et al[8] who found 45.45% as mild, 45.45% as moderate and 9.10% as severe haemophilia. Gupta et al[10] study found severe haemophiliacs constituted majority (63%), mild 14.4% and moderate 22.9%, that is not similar to our study. The increased incidence of severe haemophilia in their study is probably due to their widespread extensive study and increased number of referral cases.

This study showed the modality of treatment received by the patients. It was obvious that FFP (49 out of 100 cases) is the most common modality of treatment in HCD. Borhany et al[9] in his study reported that fresh frozen plasma, cryoprecipitate and its components were used most frequently; viral inactivated factor concentrate were used when available. In our series, coagulation profile was done in 100 cases. Almost all the patients had prolonged activated partial thromboplastin time except 1 patient of RICD. One patient of RICD had normal spectrum of coagulation profilebut the urea clot solubility test was positive. The above mentioned laboratory findings are almost similar to findings by Sahaet MM al[12] and Franchini M et al[13]. Rare inherited coagulation factor deficiencies have autosomal recessive inheritance in both genders. Hereditary FVII deficiency is the most common of RICD. RICDs are more frequent in countries like Iran, Middle East and India, where consanguineous marriages are common[14,15]. Khalid et al[16] also noted rare inherited bleeding disorders beside Haemophilia A and Haemophilia B.

Conclusion

From this study found that Haemophilia A, haemophilia B and vWD are the common encounteredinherited coagulation disorders in our populations. In Bangladesh, a lot of patients have been suffering from hereditary coagulation disorders with its complications but there is still inadequate study in our country. So this study has focused mainly to create awareness about the complications of inherited coagulation disorders and its prevention at national level. Further studies are needed to address this public health problem with a hope of improving care and harmonizing the social burden.

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