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Pathology

SPECTRUM OF INHERITED BLEEDING DISORDER IN EASTERN UTTAR PRADESH

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ABSTRACT

Introduction: Bleeding is very common symptom of a variety of disorders. It may be due to acquired or inherited. Many a time it is very difficult to know the exact cause of bleeding.

Material and Methods: This was a retrospective study to know the type of bleeding disorders in the Easter part of Uttar Pradesh. A comprehensive laboratory work up done were complete blood count, microscopic examination of peripheral blood, PT, APTT, Factor assays, vWF Ag assay and platelet studies.

Result: 57 patients presented with history of different types of bleeding symptom. Joint bleeding was the most common. Menorrhagia was the most common bleeding symptom in female of child bearing age. Family history was present in 95 % of hemophiliac patients.

Conclusion: This region showed Hemophilia as the most common type of bleeding disorders. This is in contrast to finding of normal population. This is a hospital based study and may be the reason of this type of finding.

KEYWORDS : .

Introduction

Under normal circumstances, hemostasis is tightly balanced between bleeding and thrombosis. Excessive bleeding occurs either due to acquired or inherited defects. Acquired defects occur due either to systemic illness or pharmacological interventions. Excessive bleeding may be seen in aged individual and during pregnancy. Inherited defects of bleeding are many that include abnormalities in coagulation factors (87%), platelet (8 %) and fibrinolytic system (3 %) and many remain undiagnosed (1) **.** The symptoms of bleeding disorders are different and depend upon the type of defects. There is mucosal type of bleeding in platelet abnormalities and von Willebrand Disease (vWD) while in clotting factors deficiency, the bleeding is deep intramuscular and into the major joints (2)**.** But many a times it is difficult to differentiate the cause of bleeding.

vWD is the most common type of inherited bleeding disorder with a prevalence of approximately 1 % in general population. It affects both the sexes equally (3)**.** vWD is due to qualitative and quantitative defects of vWF. In clotting factor abnormalities, hemophilia A is the most common bleeding disorder that occurs due to deficiency of factor VIII.

Material and Methods

Thus study was conducted in the division of hematology, Department of Pathology, IMS, BHU form January 2016 to December 2016. Patients comprised of ages between 5 days to 52 years. These patients were referred to the laboratory for investigation of suspected features of bleeding disorder. A detailed clinical history taken and physical examination were performed. Clinical history specifically included frequency and age of onset of bleeding, family history of bleeding, history of drug intake and indication of prior blood transfusion.

Laboratory tests performed were Complete Blood Count (CBC), microscopic examination of peripheral blood smear, Prothrombin Time (PT), Activated Partial Thromboplastin Time (APTT), Platelet aggregation study, vWF Antigen Assay, Factor VIII and Fctor IX assays.

For coagulation and platelet study blood was collected in 3.2 % sodium Citrate anticoagulant in a fixed ratio of 9:1 (9 parts blood and one part anticoagulant). Platelet rich and platelet poor plasma are prepared by centrifuging blood at 150-200 g for one minute and at 2000 g for 10 minutes respectively. PRP and PPP plasma were used for platelet and coagulation factor study respectively. EDTA anticoagulated blood was used for CBC, platelet count and microscopic examination of Leishman stained blood smear. PT and APTT were measured by standarded method, clot based assay mannualy and by semiautomated Diagnostica stago. Ristocetin Induced Platelet aggregation (RIPA) and low dose RIPA were used to know the platelet abnormality and for differention of vWD. Factor VIII and Factor IX were estimated by doing mixing experiments. vWF-Ag level was estimated by ELISA (Diagnostica stago)

Results

There were 57 patients had abnormal bleeding disorders. Patents age range from 1 month to 40 years. There were 51 males and 6 females. The overall male female ratio was 8.5/1. Overall pattern of bleeding manifestation is given in **table-1**.Out of 57 patients, 2 were of vWD, 44 Hemophilia A, 3 Hemophilia B, 1 Glanzmann thrombasthenia, 1 Factor XIII deficiency and 6 remain unclassified (**Table 2**). Hemophilia was categorized into severe (Factor VIII < 1 % of normal), moderate (Factor VIII >1% to <5% of normal) and mild (>5 % to <40 % of normal) (4)**.** Total number of hemophilia patients is shown in **table-3**. Most common symptoms in hemophilia were joint deformity followed by deep muscular bleeding. 65 % of patients had joint deformity. Most commonly affected joint is knee followed by elbow, shoulder and hip. Patients of vWD were presented with very mild to severe bleeding. Common type of bleeding was epistaxis, menorrhagia, gum bleeding, petechiae, purpura and gastro intestinal bleeding.

Discussion:

Frank bleeding with family history alongwith classical signs gives clue to the type of abnormality and can be easily diagnosed and confirmed. It is very difficult to diagnose a mild bleeding disorder and many remain undiagnosed. This is also found in the work done by Mrinalini Kotru et. al of AIIMS, Delhi (5). Exact prevalence of different types of inherited bleeding disorders in India is not known due to lack of national registry (6). Type 1 vWD is the most common inherited bleeding disorder in general population (3), but as per Ghosh k et.al, the type 3 vWD is the most common inherited bleeding disorder followed by type 1 and type 2vWD. Present study showed 2 cases of vWD.

It is important to mention here that most of the studies from India are hospital based. Thus this may not reflect the true finding of general population. The exact prevalence of inherited bleeding disorder can be derived from epidemiological study of general population. But, in India it is very difficult to do the population study because of lack of well-equipped laboratory, financial support, unawareness about the disorder. Diagnosing a bleeding disorder require battery of complex tests, repeat test at latter time, taking proper clinical history. These are the reasons why bleeding disorder remain underdiagnosed entity in India.

Now it is time to start the national registry of bleeding disorders, so that disease burden can be known in general population and timely intervention can be taken to reduce morbidity and mortality due to this.

Table-1: Pattern of bleeding symptoms

Types of bleeding	Number of Patients affected	Percentage (n=57)
Epistaxix	15	26
Gingival	25	44
Echymosis	23	40
Hemarthroses	37	65
Spontaneous	16	28
Menorrhagia	3	0.05
PPH	1	0.01
Genitourinary	28	49

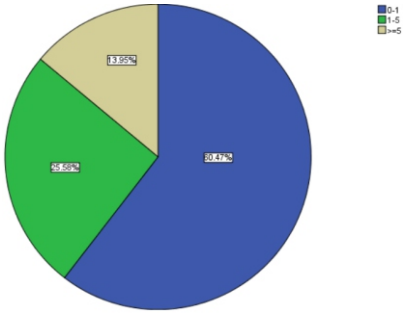
Table-2: Type of bleeding disorders

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	APLA	1	1.8	1.8	1.8
	GT	1	1.8	1.8	3.5
	HA	43	75.4	75.4	78.9
	HB	3	5.3	5.3	84.2
	UD	6	10.5	10.5	94.7
	vWD	1	1.8	1.8	96.5
	vWD s/o	1	1.8	1.8	98.2
	XIII	1	1.8	1.8	100.0
	Total	57	100.0	100.0	

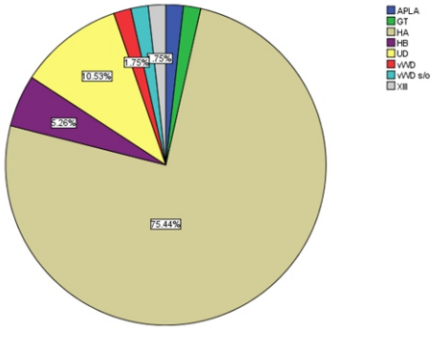
Table-3: Distribution of Hemophilia patients

Factor VIII & IX level	Frequency	Percent
0-1	28	49.1
1-5	12	21.1
>=5	6	10.5
Total	46	80.7

Pie diagram showing occurrence of hemophilia A of different severity



Pie diagram showing relative prevalence of inherited bleeding disorders



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