RARE BLEEDING DISORDERS ARE NOT SO RARE.

*M.Borhany, T. Shamsi, H.Fatima, A.Naz, H. Patel

Department of Haemostasis & Thrombosis, National Institute of Blood Disease and Bone Marrow Transplantation (NIBD), Karachi, Pakistan
*corresponding author email: drmunirashoaib@yahoo.com

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INTRODUCTION

- Globally at least 20% of the human population live in communities with a preference for consanguineous marriage and at least 8.5% of children have consanguineous parents. So consanguinity remains common in several populations around the world.
- However, consanguinity rates vary from country to country. In Pakistan, close consanguineous unions continue to be extremely common as with South West Asia.
- As a result of these marriages, autosomal recessive disorders become common. They are so frequent that they even exceed the prevalence of disorders like haemophilia B, representing an important clinical and social problem.
- **Here, we describe the frequency of rare inherited coagulation bleeding disorders, their types and clinical features among patients seeking advice for bleeding tendencies from a single centre in Pakistan.**

MATERIAL AND METHODS

- Pre-designed data sheets were filled by incorporating patients' demographics, family history, present and past history of bleeding episodes with the associated signs and symptoms. In female cases, maternal and obstetrical history was taken.
- Blood samples were collected for CBC in EDTA and 0.109M (3.2%) trisodium citrate in a ratio of 9:1 for coagulation assays. Prothrombin time (PT), activated partial thromboplastin time (APTT), fibrinogen, VWF: Ag, RiCoF and factor assays were performed. Urea clot solubility test was done in cases where all coagulation tests were normal.
- Coagulation tests were done on CA-1500 (Sysmex, Kobe, Japan), using appropriate quality control materials and standard reagents (Dade Behring, Germany).

Diagnosis	Number	Frequency
FXIII deficiency	16	33.3%
FVII deficiency	11	23%
Fibrinogen deficiency	09	18.7%
FV deficiency	05	10.4%
FX deficiency	02	4.1%
FXI deficiency	01	2.1%
Combine FV+FVIII deficiency	02	4.1%
Vitamin K dependent factor deficiency	02	4.1%

Table 1: Distribution of 48 patients with RBDs

RESULTS

- Out of 447 patients diagnosed with inherited coagulation bleeding disorders, 48 subjects had rare bleeding disorders (10.7%). Among them, 55% were male and 45% were female. Median age of all the patients was 9.8 years, (range 6 months - 27yrs).
- The most common deficiency was FXIII (n=16) followed by FVII (n=11), fibrinogen (n=9), FV (n=5), FX (n=2) and FXI deficiency (n=1), respectively. There were two cases of combined FV & VIII deficiency and 2 cases of combined vit. K depended factor deficiency (table 1).
- Clinical bleeding episodes were classified into four categories according to severity: grade III, II, and I bleeding were noted in 62.5%, 45.9%, and 10.4% patients, respectively (table 2). Gum bleeding, epistaxis, and easy bruising; menorrhagia and umbilical cord bleeding were the main clinical manifestations (Figure 1)
- Fresh frozen plasma / cryoprecipitate were used in the management of most patients.

Table 2: clinical bleeding severity	**Definition**
Asymptomatic	No documented bleeding episodes
Grade I bleeding	Bleeding that occurred after trauma or drug ingestion
Grade II bleeding	Spontaneous minor bleeding: bruising, ecchymosis, minor wounds, oral cavity bleeding, epistaxis and menorrhagia
Grade III bleeding	Spontaneous major bleeding: hematomas, hemarthrosis, CNS, GI, and umbilical cord bleeding
CNS = central nervous system, GI = gastrointestinal	

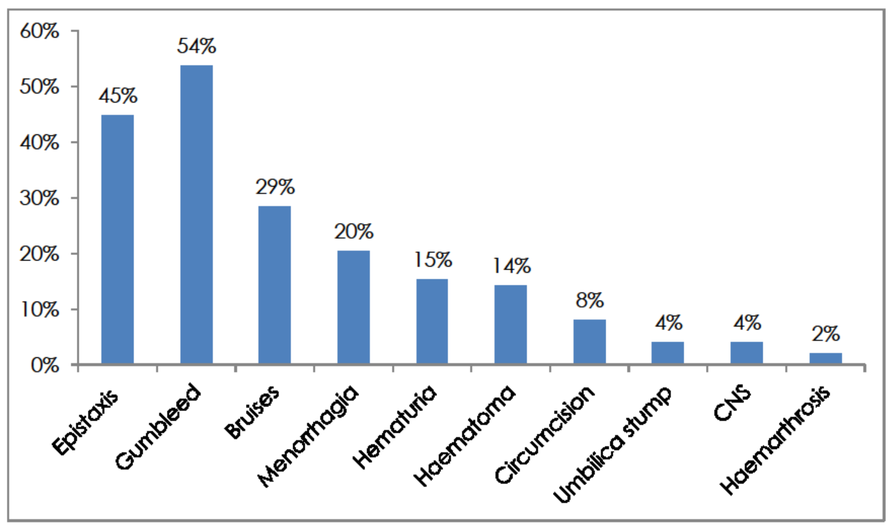

Figure 1: Type of Bleeding in Rare Inherited Bleeding Disorder patients

CONCLUSION

- The study shows that autosomal recessive disorders are common in a setting of consanguineous marriages. This keeps all the beneficial and adversely affecting recessive genes within the family; in homozygous states that results in life threatening diseases.
- Thus further studies of the association between phenotype and genotype in this subset of patients are needed to prevent the spread of such common occurrence of these rare disorders in the community.

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