Are They Really Rare?
Prevalence of Rare Bleeding Disorders (RBDs) in North East of Iran

Zahra Badiei[1], Hamid Farhangi[2], MohammadReza Keramati[3], Abdollah Banihashem[4], Ali Ghasemi[5], Elahe Yasi[6], Masoud Shahroodian[7]

1- Pediatric Hematologist-Oncologist, Hemophilia-Thalasseamia Center of Mashhad (Sarvar Clinic), Mashhad University of Medical Sciences(MUMS),Mashhad, Iran.
2- Pediatric Hematologist-Oncologist, Hemophilia-Thalasseamia Center of Mashhad (Sarvar Clinic), Mashhad University of Medical Sciences(MUMS),Mashhad, Iran.
3- Hematopathologist, Hemophilia-Thalasseamia Center of Mashhad (Sarvar Clinic), Mashhad University of Medical Sciences(MUMS),Mashhad, Iran.
4- Pediatrician, Hemophilia-Thalasseamia Center of Mashhad (Sarvar Clinic), Mashhad University of Medical Sciences(MUMS),Mashhad, Iran.
5- Pediatric Hematologist-Oncologist, Hemophilia-Thalasseamia Center of Mashhad (Sarvar Clinic), Mashhad University of Medical Sciences(MUMS),Mashhad, Iran.
6- Pediatrician, Hemophilia-Thalasseamia Center of Mashhad (Sarvar Clinic), Mashhad, Iran.
7-Laboratory Specialist, Hemophilia-Thalasseamia Center of Mashhad (Sarvar Clinic), Mashhad, Iran.

Introduction:

Deficiencies of factor VIII and factor IX are known as hemophilia A and B, respectively. Rare clotting factor deficiencies are bleeding disorders in which one or more of the other clotting factors (i.e. factors I, II, V, V+VIII,VII, X, XI, or XIII) is missing or not working properly. Less is known about these disorders because they are diagnosed so rarely. In fact, many have only been discovered in the last 40 years(1). They may present significant difficulties in diagnosis and management. (2)

The overall frequency of them in the general population is low .Homozygous deficiency varies from 1 in 500,000 for F VII deficiency to 1 in 2 million for prothrombin deficiency. The prevalence of these disorders is strongly influenced by the *racial mix in the population.*

All the disorders are autosomally inherited and with the exception of FXI deficiency, generally have *no significant clinical manifestations in heterozygotes.* The bleeding risks in affected individuals may be difficult to assess. Severe deficiencies are more likely to be found in populations where consanguineous marriage is common (like IRAN) and in rare cases individuals may inherit more than one disorder.(3)

Systematic reporting (case series) has been done from **Iran** for several disorders, although it is not clear how representative the clinical findings are for other populations and mutations.(3-9)

Here we report the number and relative prevalence of RBDs in Hemophilia - Thalassaemia Center of Mashhad (Sarvar Clinic) in north east of Iran.

Material &Methods:

Our center has begun its work from Dec 2004 and until now 95 cases of congenital rare bleeding disorders are registered in our center.

Considering that about 7000,000 residents live in Khorasan provinces (Razavi, North, and South) and according to general population prevalence it was calculated that how many cases of each RBD are expected to be found in this area and on the other hand real prevalence for each kind of RBDs is calculated.

Results:

Among 542 registered cases 371 are: hemophilia A (258),hemophilia B(62) and VWD (51). Known Platelet disorders include 30 cases (Glanzman thromboastenia 24 and Bernard- soulier 6). And 95 cases of different kind of RBDs which are shown in table.

Disorder	Prevalence In General Population According To References	Expected No Of Cases	Observed Cases And Real Prevalence In Our Region
FV+VIII	1/1000,000	7	30 (1/230,000
FVII	1/500,000	14	22 (1/300,000)
FV	1/1000,000	7	17 (1/400,000)
FXIII	1/1000,000	7	10 (1/680,000)
FI	1/1000,000	7	7 (1/1000,000)
FX	1/1000,000	7	2 (1/3,500,000)
FII	1/2,000,000	3-4	2 (1/3,500,000)
FXI	1/100,000	70	0 ?

Conclusion:

It seems that in area like Iran that consanguineous marriage is common, most of these disorders are not as rare as previously thought and for correct and in-time diagnosis of these disorders having a high clinical suspicion is important. And when a case is diagnosed in a family , good history should be taken from another members of family for finding any more possible cases.

References:

1. *Bolton-Maggs P. H. B., Perry D. J., Chalmers E. A.et al. The rare coagulation disorders – review with guidelines for management from the United Kingdom Haemophilia Centre Doctors' Organization. Haemophilia (2004), 10, 593–628*
2. *What are Rare Clotting Factor deficiencies? Published by the World Federation of Hemophilia, 2009*
3. *Bolton-Maggs P. H. B . Treatment of Hemophilia ;The Rare Coagulation Disorders : Published by the World Federation of Hemophilia April 2006 • NO 39*
4. *Lak M, Keihani M, Elahi F, Peyvandi F,Mannucci PM. Bleeding and thrombosis in 55 patients with inherited afibrinogenaemia.Br J Haematol 1999; 107:204-6.*
5. *Lak M, Peyvandi F, Ali Sharifian A, Karimi K, Mannucci PM. Pattern of symptoms in 93 Iranian patients with severe factor XIII deficiency. J Thromb Haemost 2003; 1:1852-3.*
6. *Lak M, Sharifian R, Peyvandi F, Mannucci PM. Symptoms of inherited factor V deficiency in 35 Iranian patients. Br J Haematol 1998; 103:1067-9.*
7. *Peyvandi F, Mannucci PM, Asti M, et al.Clinical manifestations in 28 Italian and Iranian patients with severe factor VII deficiency. Haemophilia 1997; 3:242-246.*
8. *Peyvandi F, Mannucci PM, Lak M, et al.Congenital factor X deficiency: spectrum of bleeding symptoms in 32 Iranian patients.Br J Haematol 1998; 102:626-8*
9. *Peyvandi F, Tuddenham EG, Akhtari AM,Lak M, Mannucci PM. Bleeding symptoms in 27 Iranian patients with the combined deficiency of factor V and factor VIII. Br J Haematol 1998; 100:773-6.*

DOI: 10.3252/pso.eu.WFH2012.2012