Von Willebrand disease type 3: Reporting novel mutations

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Introduction:
Von Willebrand’s disease (VWD) is the most common hemorrhagic disorder and is created by quantitative (types 1 and 3) or qualitative (types 2A, 2B, 2M, 2N) deficiency of von Willebrand factor (VWF). Von Willebrand disease type 3 (VWD type 3) is a dominant/recessive autosomal inherited bleeding disorder caused by quantitative or qualitative defects of von Willebrand factor (VWF). The VWF is a blood clotting protein which is encoded by VWF gene. This study presents molecular genetic analysis on VWD type 3 which is the most severe form of this disease.

Materials and methods:
A total of 25 individuals diagnosed with autosomal recessive Von Willebrand disease type 3, were selected from patients referred to Kawsar Human Genetics Research Center. Sanger sequencing were used to directly sequence all exons and intron-exon boundaries of the VWF gene in 8 families.

At first, genetic counselling is done by a doctor in this center. Then 5-10ml blood sample is prepared from the participants and pouring it to the EDTA containing container with the aim of DNA extraction by using of salt-extraction method and Boiling. Sequencing method is used for genotyping of the samples. All samples were analysed for Short Tandem Repeat (STR) and Restriction Fragment Length Polymorphism (RFLPs) by using of appropriate primers. Mutation detection in other families is in progress with targeted next generation sequencing.

Result and Discussion:
A total of 6 different mutations were identified in exons 16, 20, 26, 30, 37 and 45 among investigated patients. All mutations were novel. In silico studies and segregation analysis confirmed pathogenicity of these mutations.

Until now only few studies have performed on VWD type 3 in Iran. Different problems in patients affected by this disorder can show importance of these studies in different countries. More studies with larger samples can help to detect the most common mutations in the VWF gene which is useful for genetic diagnosis of this disease.

Key Words:
Von Willebrand Factor, von Willebrand disease type 3, VWF gene, Iran

Reference: