Abstract ID: - 201

Abstract Topic: - Clinical Genetics

Abstract Title: - In silico analysis of a novel non-synonymous missense mutation in UROS gene associated with hereditary Congenital Erythropoietic Poryphyeria.

Presenting author name: - Aishwarya R Nair

Presenting author institute: - Institute Of Genetics and Hospital for Genetic Diseases

Co-authors name: - Reshma Taj, Rinku Varghese, Pavani Ayyadevara, Srinath Buragadda, Sunita Tella, Vijaya L.Bodiga, , ,

Co-authors institute: - Institute of Genetics and Hospital for Genetic Diseases, Vellore Institute of Technology, Institute of Genetics and Hospital for Genetic Diseases, Institute of Genetics and Hospital for Genetic Diseases, Institute of Genetics and Hospital for Genetic Diseases, Institute of Genetics and Hospital for Genetic Diseases, , ,

Aims: - Congenital erythropoietic porphyria (CEP) is a rare autosomal recessive cutaneous porphyria affecting less than 1 in 1,000,000 children. This inborn error of heme biosynthesis is caused by mutations in the gene coding for uroporphyrinogen III synthase (UROS). This cytosol localized enzyme catalyzes the conversion of hydroxymethylbilane into uroporphyrinogen I which cannot be metabolized into heme and its accumulation in red blood cells results in intramedullary and intravascular haemolysis. Compound homozygous mutations in this gene are preferably encountered in consanguineous families. The condition is typically manifested in early childhood with distinct clinical symptoms of variable severity. With few cases reported and barely on the probable protein changes ensuing after the mutation, we report a case in a one-month-old baby, born to a consanguineous couple, from the local area. The baby showed clinical indications of sepsis, photosensitivity, respiratory distress, and anaemia. The DNA was subjected to clinical exome sequencing and reported to have a homozygous missense variation in exon 10 of the UROS gene, c.791T>C(p.Leu264Pro). Earlier studies reported amino acid change at 237th position, but this change Leu264Pro is novel and no protein structural effects were reported. We proposed to perform structure prediction, conservation analysis, pocket identification, and docking interactions, and the effect of mutation on this novel mutation.

Methods: - Clinical Exome Sequencing,In Silico Analysis,Softwares for protein docking , structure predictions.

Results: - The in silico results showed poor enzymatic activity as consequence of this mutation compared to the wild type and previously reported mutation(L237P) in German population.

Conclusions: - In-silico analysis results demonstrated that the mutation produced notable changes in the normal structure conformation and in the protein interaction site which subsequently resulted change in its interaction with substrate leading to loss of function.

Keywords: - The in silico results showed poor enzymatic activity as consequence of this mutation compared to the wild type and previously reported mutation(L237P) in German population.