OP 05 - Identification of Val162del pathogenic variant of the *SLC40A1* gene associated with Hereditary Hemochromatosis type 4 in a cohort of iron overload patients

M. A. Dharmaratne[1*], T. K. Wetthasinghe[1], N. Noordeen[1], V. H. W. Dissanayake[1]

[1]Human Genetics Unit, Faculty of Medicine, University of Colombo, Colombo 08, Sri Lanka

Introduction: Hereditary hemochromatosis type 4 is as an autosomal dominant iron overloading disorder associated with variants of the SLC40A1 gene, that encodes the only known iron exporter, ferroportin (Fpn). The Val162del pathogenic variant has been commonly reported from Asian populations and is categorized as a loss-of-function variant. These variants are associated with hyperferritinemia and low to normal transferrin saturation in affected individuals. Hereditary hemochromatosis type 4 has a high phenotypic heterogeneity. This study aims to design and implement a genotyping assay for the Val162del variant in a cohort of patients with iron overload symptoms.

Methods: The study cohort included 47 patients with suspected iron overload symptoms who had priorly consented for such studies. The genotyping was performed for the Val162del (rs878854984) pathogenic variant by a novel tetra-amplification refractory mutation system (T-ARMS) polymerase chain reaction that was implemented, optimized and validated by Sanger sequencing.

Results: The Val162del pathogenic variant was not detected in this study cohort. All 47 patients were found to carry the ancestral allele (GTT) with a major allele frequency of 1 and a minor allele frequency of 0. 31.7% of the male subjects and 50% of the female subjects presented with symptoms during the 5th and 6th decade of life.

Conclusion: In conclusion, a novel genotyping assay has been successfully designed to detect the Val162del pathogenic variant. However, Val162del does not appear to be prevalent in the selected study. Further studies using larger cohorts needs to be conducted to determine the association of this pathogenic variant in our population.

Keywords: Hereditary hemochromatosis, ferroportin, hyperferritinemia, tetra-amplification refractory mutation system

*Email: bmsalex94@gmail.com