Preliminary genetic analysis of selected PYGL variants in two children with Glycogen Storage Disease Type VI in Sri Lanka

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Glycogen Storage Disease Type VI (GSD VI), or Hers disease, is a rare autosomal recessive metabolic disorder resulting from pathogenic variants in the *PYGL* gene, which encodes liver glycogen phosphorylase, an essential enzyme in glycogenolysis. Despite its clinical significance, the genetic landscape of GSD VI remains largely unexplored within the Sri Lankan population. The current study aimed to conduct a preliminary molecular investigation by screening three selected *PYGL* variants: c.280C>T, c.434T>G, and c.1620+1G>A in two pediatric patients clinically diagnosed with GSD VI. Genomic DNA was extracted from peripheral blood samples, followed by primer design, polymerase chain reaction (PCR) optimization, and Sanger sequencing. Both patients presented with classical clinical features, including hepatomegaly and elevated hepatic transaminases; however, none of the targeted *PYGL* variants were identified in either patient. These findings suggest potential genetic heterogeneity and the likelihood of uncharacterised or novel *PYGL* mutations within the Sri Lankan cohort. The current study can be extended to develop a mutation spectrum for GSD VI, thereby improving genetic testing and counselling, which may assist in treatment management for affected individuals in Sri Lanka.

Keywords: *Glycogen Storage Disease (GSD), GSD Type VI, PYGL gene, Liver glycogen phosphorylase and hepatomegaly*