PREVALENCE OF THE *NEUROD1* H241N MUTATION AND ITS ASSOCIATION WITH GENETIC PREDISPOSITION TO TYPE 2 DIABETES IN A SRI LANKAN COHORT

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Abstract

Type 2 Diabetes Mellitus (T2DM) is a growing metabolic disorder characterized by insulin resistance and impaired beta-cell dysfunction, with a particularly high prevalence in South Asia, including Sri Lanka. While T2DM is primarily a polygenic disease, monogenic forms of diabetes such as maturity-onset diabetes of the young (MODY), including MODY6 caused by mutations in *NEUROD1*, may present with overlapping clinical features and are therefore susceptible to misclassification as T2DM. The *NEUROD1* H241N variant (c.723C>G; p.His241Asn) occurs at 4% frequency in a Sri Lankan MODY cohort, versus 0.6% among South Asians generally, and is absent in non-Asian populations, having been classified likely pathogenic in Asian studies. Given the MODY–T2DM overlap and Sri Lanka's substantial T2DM burden, this study assessed its prevalence and association with T2DM. The study was conducted using buccal swab samples from 36 individuals (n=36). Genomic DNA was extracted and PCR amplification performed targeting the *NEUROD1* c.723 position. Products were verified by agarose gel electrophoresis and analyzed by Sanger sequencing. Of the 36 samples, 30 met the quality thresholds, yielding a final cohort of 15 T2DM patients and 15 non-diabetic controls. Sequence alignment was performed using the Ensembl annotation of *NEUROD1* (ENSG00000162992), with the corresponding RefSeq transcript NM_002500.4, using BioEdit Sequence Alignment Editor (v7.0.9). Analysis revealed no nucleotide substitution at the c.723C position in any sample, confirming the absence of the *NEUROD1* H241N variant in both groups. These findings do not show a specific association of *NEUROD1* H241N variant with T2DM. This pilot study was limited by a small sample size. Despite its reported high frequency in previous MODY cohorts, this variant was absent among the 30 T2DM patients and healthy controls analyzed, warranting further investigation into its relevance to diabetes pathogenesis.

Keywords: Type 2 Diabetes Mellitus, *NEUROD1*, H241N variant, c.723C>G, MODY6