

**ABSTRACT****The Nature and Prevalence of Maturity-Onset Diabetes of the Young (MODY) in Trinidad****Laura-Lee Gita Boodram**

The incidence of diabetes mellitus in Trinidad and Tobago is high, affecting approximately 11% of adults 35 years and older. However, the genetic factors underlying the inheritance of diabetes in this population are largely unknown. Maturity-Onset Diabetes of the Young (MODY), a monogenic form of diabetes mellitus, is characterised by an early age of onset (< 25 years), an autosomal dominant mode of transmission and a primary defect in insulin secretion. This study estimated the prevalence of MODY among early-onset diabetic patients in the Trinidadian population.

Two hundred and sixty four early-onset diabetics, belonging mainly to the South-Asian and African groupings, were screened for mutations in the coding regions of the hepatocyte nuclear factor-1 $\alpha$  (HNF-1 $\alpha$ ), glucokinase (GCK), insulin promoter factor-1 (IPF-1), and neurogenic differentiation factor-1 (NeuroD1) genes.

Putative diabetogenic mutations were discovered in approximately 3.4% of the study population. Three novel mutations were detected in the HNF-1 $\alpha$  gene, A14E, P290H, and L389V. One previously reported mutation, E224K, was discovered in the IPF-1 gene, and two novel mutations were detected in the NeuroD1 gene, P204S and A251S.

Functional studies conducted on the A14E, P290H and L389V mutations revealed that the A14E mutant protein showed a  $27.0 \pm 3.0\%$  ( $P < 0.005$ ) decrease in transactivation function and a  $16.8 \pm 1.8\%$  ( $P < 0.001$ ) decrease in DNA binding capacity when compared to wild type HNF-1 $\alpha$ . The P290H and L389V mutants displayed activities similar to the wild type. The A14E mutation appears to co-segregate with diabetes mellitus within the affected pedigree. Carriers of the mutation display a decrease in pancreatic  $\beta$ -cell function.

It was concluded that MODY, although present in the Trinidadian population, is not a major contributor to the prevalence of diabetes mellitus. Nevertheless, promoting awareness of this form of diabetes locally would lead to the early detection and treatment of affected families.

Key words: Trinidad, early-onset type 2 diabetes, Maturity-Onset Diabetes of the Young (MODY), South-Asian, African, HNF-1 $\alpha$ , glucokinase, IPF-1, NeuroD1.