

Exploring Strategies to Detect MODY In an Emirati Population

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Background:

Maturity-onset diabetes of the young (MODY) has been reported sporadically in the UAE. The MODY probability calculator (MPC), developed in white European individuals, uses basic clinical data to calculate the positive predictive value (PPV) of individuals for finding MODY.

Aims:

We assessed the performance of the MPC in an Emirati population.

Methods:

We recruited individuals diagnosed with any type of diabetes <30 years from a diabetes clinic (Cohort-1), Imperial College London Diabetes Centre (ICLDC). We applied the MPC to pancreatic antibody negative individuals and selected those with a PPV $\geq 62.4\%$ for testing of all MODY genes, using targeted next generation sequencing. Subsequently, we retrospectively calculated PPVs in genetically confirmed MODY cases from clinic, selected for genetic testing by their clinician (Cohort-2).

Results:

Cohort-1: 240 of 644 individuals scored PPV $\geq 62.4\%$. 68 of 240 individuals with a PPV $\geq 62.4\%$ (86% had PPV $\geq 75.5\%$) were genetically tested. Of these, 4.4% (3/68) were found to harbour MODY mutations in HNF1A or HNF4A. Cohort-2: 15 individuals were identified with pathogenic mutations in HNF1A, HNF1B, GCK or INS. 73% (11/15) had a PPV $\geq 62.4\%$ and 27% (4/15) scored PPVs $\geq 21 - 62.4\%$. The individuals with confirmed MODY who scored $< 62.4\%$ were insulin- treated from diagnosis (n=2), were obese (n=1) or were older with higher HbA1c (n=1). Comparing the phenotype of MODY cases (n=14) vs no MODY (n=65), in those with PPV $\geq 62.4\%$; MODY cases were significantly leaner (BMI 21.8 vs 26.2 kg/m² p=0.01), but age-at-diagnosis (14.7 vs 17 years p=0.72), duration (6.2 vs 7.7 years p=0.68) and HbA1c (8.8% vs 7.3% p=0.10) were not significantly different. No differences in treatment modality or parental history were observed.

Conclusions:

The MPC overestimates the pre-test probability for a significant proportion of Emiratis. The 96% who tested negative for MODY had features consistent with young-onset type 2 diabetes. 27% of our confirmed MODY cases had lower PPVs due to atypical features. The MPC requires ethnic-specific refinement to take account of variable diabetes phenotypes in the UAE.