



EVALUATING CLINICAL MARKERS TO IMPROVE SELECTION OF DIABETES PATIENTS FOR GENETIC TESTING



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Introduction

MODY is a form of monogenic diabetes typically characterized by early onset, non-insulin dependence, and an autosomal dominant inheritance pattern. However, less than 50% of MODY patients present with this classic clinical profile. This variability largely reflects the number of genes associated with this condition and the fact that each patient's phenotype depends on the role of the affected gene in glucose metabolism. As a result, MODY is frequently misdiagnosed as type 1 or type 2 diabetes, increasing the challenge for clinicians to correctly identify and treat affected individuals. Accurate identification of these cases is essential, as it enables clinicians to design treatment more appropriately and ultimately improve the patient's health prognosis. The identification of a reliable biochemical marker that could help clinicians recognize potential MODY cases—later confirmed by genetic testing—would significantly enhance the efficiency and cost-effectiveness of MODY screening. Several biomarkers have been proposed, including autoantibodies, C-peptide, high-sensitivity C-reactive protein (hs-CRP) and lipid profile.

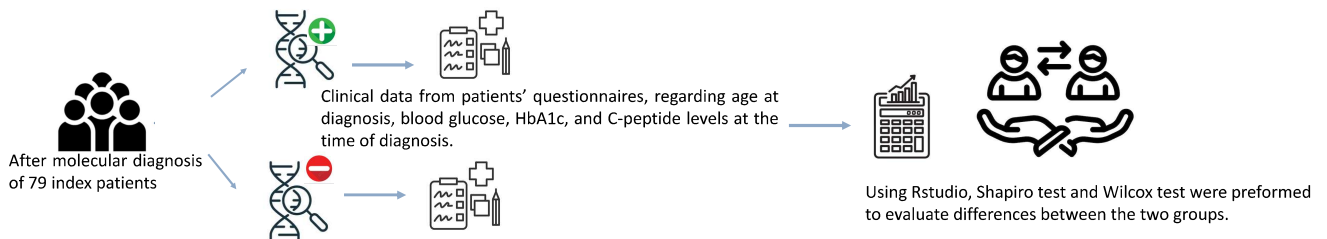
The “Molecular Study of Monogenic Diabetes” project, approved by the INSA Ethics Committee (NI 136-2023, 11/04/2023), was established to identify patients with monogenic diabetes. All participants provided a blood sample, completed a clinical questionnaire, and signed informed consent. To date, 79 index cases with diabetes have been screened for pathogenic variants in the *GCK*, *HNFI1A*, *HNFI1B*, and *HNFI4A* genes, which together account for more than 90% of MODY cases.



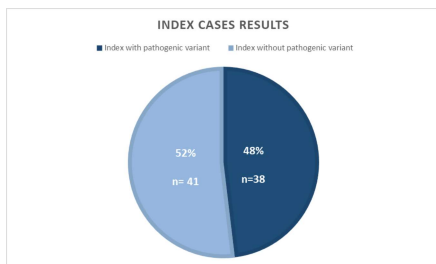
Our aim:

Compare the phenotype between index cases with and without MODY variant based on the clinical data collected from the clinical questionnaires to see if any distinguishable features would stand out and facilitate the early identification of MODY individuals.

Methods



Results



	MODY cases (MV±SD)	Negative cases (MV±SD)	Wilcox Test (p value)
Mean value of initial glycemia (mg/dl)	171,3 ±111,5 (n=30)	200,4 ±121,4 (n=27)	0,2939
Mean value of initial HbA1C (%)	7,1±2,0 (n=30)	7,9±2,4 (n=26)	0,1717
Mean value of C peptide (ng/ml)	2,5±1,6 (n=17)	2,1±1,4 (n=17)	0,558
Mean value of diagnosis age (years)	14,6±5,9 (n=36)	18,7±8,7 (n=41)	0,0324

Table 1 Statistical analysis results: comparison between MODY cases and Negative cases. MV – mean value. SD –Standard deviation. Statistical significance was set at p value < 0.05

Discussion

- Blood glucose, HbA1c, and C-peptide levels at diagnosis **did not differ significantly** between groups, suggesting that these parameters alone are not sufficient to clearly distinguish MODY from negative cases.
- The **MODY group was diagnosed at a younger age**, likely due to the high proportion of GCK-MODY individuals in our cohort:
 - GCK-MODY is characterized by mild, stable hyperglycaemia present from birth, which facilitates earlier detection.
 - In contrast, other MODY subtypes typically show progressive hyperglycaemia and are therefore diagnosed later.
- Phenotypic characterization has limitations:
 - Only 37.9% of index cases with complete genetic analysis provided full responses to the clinical questionnaire.
 - Only three biomarkers were analyzed, which may restrict the depth of comparison.
- Despite these limitations, our findings are broadly consistent with the current literature and reinforce the distinct presentation pattern of GCK-MODY cases.
- Although clinical features may raise suspicion, genetic testing is the only definitive way to confirm a MODY diagnosis.

References



Information about MODY Diabetes Study

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