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# INsight

## MODY in Latin America

Maturity Onset Diabetes of the Young (MODY) is an early onset monogenic diabetes. Despite MODY patients presenting with features and treatment requirements different from other types of diabetes, it is commonly misdiagnosed as type 1 or type 2 diabetes. MODY is an autosomal dominant inherited disorder caused by β-cell dysfunction, characterised by a vast range of different phenotypes due to genetic heterogeneity. In fact, 14 genes have been associated with MODY phenotypes which reinforces the importance of genetic testing. Heterozygous pathogenic variants in the GCK, HNF1A, HNF4A, and HNF1B genes are the four most common causes of this type of diabetes.

Due to genetic heterogeneity, it is quite common to find different clinical features in patients with MODY. Depending on genetic etiology, the different subtypes differ in terms of age of onset, pattern of hyperglycemia, response to treatment, and extra-pancreatic manifestations. However, most patients with this type of diabetes usually have low insulin requirement. They are often characterized by a strong family history of diabetes of any type, absence of evidence of β-cell autoimmunity and the presence of C peptide which indicates the production of endogenous insulin, even though patients have diabetes features. Despite all these standard features allowing suspicion of a MODY phenotype, genetic testing is needed to ensure a correct diagnosis and identify the related gene and variants, important to define the best therapeutic choice.

MODY or monogenic diabetes has a prevalence of 1-2% of all diabetes cases. However, this percentage is thought to be underestimated, as more cases of MODY have been identified in several countries in Latin America, although there are only a few studies, primarily from Brazil and Mexico. On the other hand, Latino population is one of the populations with the highest prevalence of diabetes. "*Genetic testing is not a common routine, so there is not a sufficiently robust epidemiological assessment to provide prevalence data*", tell us Dr. Lenita Zajdenverg, Diabetes and Nutrology Section leader from Federal University of Rio de Janeiro, Brazil. "*There are specific populations genotyping studies that have already been done in Rio de Janeiro and São Paulo, but there is no national prevalence. Although referral centers are aware of MODY, more basic health care facilities do not even hypothesize this diagnosis*." This highlights the great need to disseminate research in monogenic diabetes and genetic testing, so that, in the future it will be possible to obtain prevalence data.

Some studies show that mutations in the GCK gene are responsible for the majority of MODY cases in Brazil. However, it is important to note that this data may be conditioned by current diagnostic procedures. Dr. Mário Campos, a research leader in MODY at the Oswaldo Cruz Institute, Rio de Janeiro, explained: "*We conduct several molecular analyses based on selection criteria and patients´ clinical profile to determine de cause of MODY. However, despite these efforts, diagnosis remains a significant challenge. This diagnosis is not possible in a public health system except for patients followed up in university environments. Nevertheless, MODY diagnosis has been recently possible in a private system in several state capitals in Brazil. However, due to the high cost, these services are inaccessible to most people*".

For this reason, monogenic diabetes – specially in its rare forms – remains poorly studied and many patients are misdiagnosis or have an inconclusive diagnosis.

A correct and precise diagnosis is crucial for best treatment choice. It is still not completely clear what is the best therapeutic option for many genetic alterations on MODY-associated genes, particularly the rarest forms. Furthermore, some individuals may not need to use insulin therapy – a common treatment for diabetic patients.

Due to the limited molecular characterization and studies on MODY, there's a need to enhance access and improve molecular diagnostics for various MODY subtypes. Dr. Mário Campos explained, "*Implementing NGS (Next Generation Sequencing) techniques can enable faster and more accurate diagnoses. Additionally, conducting more extensive testing on a larger patient population can provide incidence data and a better understanding of each gene's contribution to the molecular causes of MODY, leading to more comprehensive and expedited knowledge acquisition*".

Moreover, there are additional challenges related to the healthcare access conditions in the country. "*Any chronic conditions faces barriers to healthcare due to the socio-economic conditions of a developing country like Brazil. Many patients have difficulty accessing and adhering to treatment*" – tell us Dr. Lenita Zajdenverg – This underscores the importance of increased investment in healthcare in Brazil.

Providing personalized treatment approaches according to individuals features may prevent or attenuate diabetes-associated health complications resulting in patients' lifestyle improvement.


References

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**Miguel Ferreira**

miguelferreira@latam.bio