Conference Proceedings By
United Research Forum, London, UK

ORGANIZED BY
UNITED RESEARCH FORUM
(CONNECT WITH RESEARCH WORLD)

5th International Conference on
Pediatrics and Neonatal Care
July 21-22, 2026 | Vienna, Austria

Rasheeba Nizam[1], Sindhu P Jacob[1], Sumi john[1], Saira Abraham[1], **Fahd Al-Mulla[1*]**

[1]Department of Translational Research, Dasman Diabetes Institute, Kuwait.

Monogenic Diabetes in Kuwait: A Comprehensive Genomic Characterisation from the Dasman Diabetes Institute with ClinGen-Guided Variant Curation

Background & Aims

Monogenic diabetes, encompassing Maturity-Onset Diabetes of the Young (MODY) and other single-gene forms, represents a clinically and genetically heterogeneous group of disorders frequently misdiagnosed as type 1 or type 2 diabetes. Accurate molecular diagnosis is critical for precision management and familial counselling. Despite its recognised prevalence, data from Arab and Middle Eastern populations remain scarce. The Translational Research Department at the Dasman Diabetes Institute (DDI), Kuwait, in collaboration with the Clinical Genome Resource (ClinGen), undertook systematic genetic characterisation of monogenic diabetes cases to define the mutational landscape in this understudied population.

Methods

Seventeen individuals with clinical suspicion of monogenic diabetes were enrolled at the DDI-National Research Centre (DDI-NRC). Comprehensive next-generation sequencing panels targeting established MODY and monogenic diabetes genes were performed. Variant classification adhered to ACMG/AMP guidelines, and ClinGen-approved variant curation frameworks were applied to ensure standardised pathogenicity assessment. Clinical data including age at diagnosis, BMI, HbA1c, autoantibody profile (GAD, IA2, ZnT8), and ethnicity were systematically recorded.

Results

A total of 17 cases (predominantly Arab ethnicity) harbouring variants across 11 distinct genes were identified. Confirmed or likely MODY subtypes included: MODY 2 (GCK, n=2), MODY 3 (HNF1A, n=2), MODY 4 (PDX1, n=1), MODY 6 (NEUROD1, n=2), MODY 7 (KLF11, n=1), MODY 12 (ABCC8, n=3), and MODY 13 (KCNJ11, n=1). Additional cases involved HNF4A, FOXP3, WFS1, NEUROG3, and a complex digenic case harbouring both PAX4 and GLIS3 variants. Notably, one neonate (3 months) presented with autosomal recessive hyperinsulinaemic hypoglycaemia of infancy, carrying a large chromosomal region of homozygosity (ROH, Chr11: 18,288,503–34,533,111) encompassing a homozygous ABCC8 exons 1–22 deletion (pathogenic, NMD) alongside a RFX6 variant (VUS). The majority of variants (12/17 index cases) were novel, with minor allele frequencies below 0.01 or absent from population databases. Pathogenicity classifications ranged from Pathogenic to Variants of Uncertain Significance (VUS), with ClinGen curation providing standardised evidence weighting (PM1, PM2, PP2, PP3, PS1, PM5, BS3, BS4 criteria). Ages at diagnosis spanned from 3 months to 33 years (median ~13 years), and HbA1c ranged from 5.7% to 14.1%, reflecting broad phenotypic heterogeneity. Three cases demonstrated positive autoantibodies (GAD+, IA2+, or ZnT8+), highlighting the diagnostic complexity and risk of misclassification as autoimmune diabetes.

https://doi.org/10.51219/URForum.2026.Fahd-Al-Mulla

ISBN: 978-1-917892-44-5

Conclusions

This study presents one of the largest monogenic diabetes cohorts from Kuwait and the broader Arab world, identifying a high proportion of novel variants across a diverse gene spectrum. ClinGen-guided curation proved essential for standardised variant interpretation, particularly in a population with limited reference data. These findings underscore the importance of molecular diagnosis in paediatric and young-onset diabetes, with direct implications for precision therapy (e.g., sulfonylurea use in ABCC8/KCNJ11 cases, dietary management in GCK-MODY), and highlight the urgent need for population-specific genomic databases in the Middle East.

Keywords: Monogenic diabetes, MODY, ClinGen, variant curation, Arab population, Kuwait, paediatric genomics, precision medicine, Dasman Diabetes Institute

Biography

Professor Fahd Al-Mulla is the Chief Scientific Officer (CSO) of Dasman Diabetes Institute (DDI) and heads the department of Translational Research. He has made profound contributions in the fields of diabetes research and genomic medicine. With an impressive portfolio of 10 patents and over 345 publications in esteemed journals such as Cell, Nature Genetics, Science, and Nature, he stands among the top 2% of the most cited scientists worldwide (h-index:61, i10-index:215).

Prof. Al-Mulla's pioneering work in cancer metastasis has been foundational, revealing critical insights into genetic heterogeneity within and between primary tumors and their metastases. He identified and characterized key metastasis suppressor genes, including Carbonyl Reductase and Raf Kinase Inhibitory Protein, substantially advancing our understanding of cancer biology.

https://doi.org/10.51219/URForum.2026.Fahd-Al-Mulla

ISBN: 978-1-917892-44-5