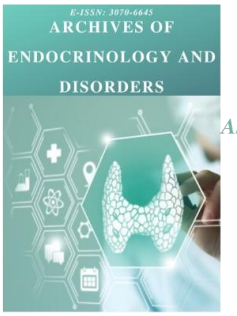

E-ISSN: 3070-6645
*Archives of Endocrinology and Disorders*

ATHENAEUM SCIENTIFIC PUBLISHERS

*Case Report*

Check for updates

# *BLK* Gene Mutation with Maturity Onset Diabetes of Young 11: First Case Report from Karnataka, India

**R Anil Kumar[1*], Arunkumar Sidri[2]**

[1]Professor and HOD, Diabetes and Endocrinology, Karnataka Institute of Endocrinology and Research, Bengaluru, India
[2]Senior Resident, Post MD Fellowship in Diabetology, Karnataka Institute of Endocrinology and Research, Bengaluru, India
***Correspondence author:** R Anil Kumar, Professor and HOD, Diabetes and Endocrinology, Karnataka Institute of Endocrinology and Research, Bengaluru, India; Email: r.anil_kumar@yahoo.co.in

Citation: Kumar RA, et al. *BLK* Gene Mutation with Maturity Onset Diabetes of Young 11: First Case Report from Karnataka, India. Arch Endocrinol Disord. 2026;2(2):1-7.

https://doi.org/10.46889/AED.2026.2202

Received Date: 14-05-2026

Accepted Date: 29-05-2026

Published Date: 06-06-2026



## Abstract

Maturity-Onset Diabetes of the Young (MODY) is a form of monogenic diabetes characterized by autosomal dominant inheritance, non-ketotic diabetes and beta-cell dysfunction, typically manifesting before 25 years of age. The clinical criteria for identifying this form of diabetes were famously coined by researchers Robert Tattersall and Stefan Fajans in the mid-1970s. The first MODY gene glucokinase was discovered in 1992 in 16 French families. MODY has been divided into 14 subtypes. MODY3 (*HNF1A*), MODY 2 (Glucokinase), MODY1 (*HNF4A*) and MODY 5 (*HNF1B*) are the most common. Mutations in the B Lymphocyte Tyrosine Kinase (*BLK)* locus are very rare. It is an important point that the number of cases with this MODY type, which is defined as BLK 1 mutation, in other words MODY 11, is very low. Bulus et.al from Turkey has reported a case of BLK gene mutation in a 17 year old patient in a case report published in annals of clinical case reports in February 2023. Borowiec, et al., reported that mutations in BLK caused diabetes in three families. We report a case of 27 years male BLK gene mutation MODY 11 diabetes. This is the first case reported from Karnataka India.

**Keywords:** Maturity-Onset Diabetes of the Young (MODY); Diabetes; *BLK* Gene; *HNF1A*; Glucokinase

## Introduction

MODY (Maturity Onset Diabetes of the Young) is a type of diabetes that has an autosomal dominant inheritance pattern and is caused by monogenic abnormalities in cell activities [1]. Tattersall and Fajans criteria for MODY were: young age at onset (<25 years), absence of ketosis, strong family history of diabetes in three or more generations, autosomal dominant inheritance and response to oral drugs for at least 5 years [2]. The first MODY gene glucokinase was discovered in 1992 in 16 French families [3]. Some of the molecular pathways that cause MODY have been clarified in recent year's improved genetic approaches.

MODY is caused by at least fourteen separate genes and various mutations have been discovered [4]. MODY, like many other genetic diseases, is inherited in an autosomal dominant pattern and refers to a collection of disorders with a wide range of genetic, metabolic and clinical features [5]. MODY has been divided into 14 subtypes, each with its own set of symptoms in terms of gene mutation, age of onset, therapy and hyperglycemia pattern [6].

Mutations in the genes Hepatocyte Nuclear Factor 4 Alpha (HNF4A), Glucokinase (GCK) and Hepatocyte Nuclear Factor 1 Alpha

(HNF1A) cause the most common types [7]. The most common MODY forms are also the ones that are termed as "actionable MODY" because they either respond to sulfonylureas [MODY3 (*HNF1A*) and MODY1 (*HNF4A*)], do not require any treatment [MODY 2 ( GCK )] or are associated with extrapancreatic features [MODY 5 (HNF1B)] [8]. A new type of MODY ABCC8 LOF mutation was discovered by V Mohan, et al., which did not respond to sulfonylureas (Table 1) [9].

| MODY gene | Frequency (% in MODYs) | Pathophysiology | Other features | Possible treatment |
|---|---|---|---|---|
| *HNF4α* | 5 | β-Cell dysfunction | Neonatal diabetes, hyperinsulinemic hypoglycemia during infancy, low triglycerides | Sensitive to sulfonylurea |
| *GCK* | 15–20 | Glucose sensing defect | Stable mild fasting glucose | No medication, or Diet |
| *HNF1α* | 30–50 | β-Cell dysfunction | Glucosuria | Sensitive to sulfonylurea |
| *PDX1* | <1 | β-Cell dysfunction | Homozygote: permanent neonatal diabetes, pancreas agenesis | Diet or OAD or insulin |
| *HNF1β* | 5 | β-Cell dysfunction | Renal malformations, genito-urinary tract anomalies, pancreatic hypoplasia, low birth weight | Insulin |
| *NEUROD1* | <1 | β-Cell dysfunction | Neonatal diabetes, child or adult-onset diabetes neurological abnormalities. | OAD or insulin |
| *KLF11* | <1 | β-Cell dysfunction | Similar to type 2 diabetes | OAD or insulin |
| *CEL* | <1 | Pancreas endocrine and exocrine dysfunction | Exocrine dysfunction, lipomatosis | OAD or insulin |
| *PAX4* | <1 | β-Cell dysfunction | Ketoacidosis-prone | Diet or OAD or insulin |
| *INS* | <1 | Insulin gene mutation | Neonatal diabetes, child or adult-onset diabetes | OAD or insulin |
| *BLK* | <1 | Insulin secretion defect | Overweight, relative insulin secretion failure | Diet or OAD or insulin |
| *ABCC8* | <1 | ATP-sensitive potassium channel dysfunction | Homozygote: permanent neonatal diabetes, Heterozygote: transient neonatal diabetes | OAD (sulfonylurea) |
| *KCNJ11* | <1 | ATP-sensitive potassium channel dysfunction | Homozygote: neonatal diabetes | OAD or insulin |
| *APPL1* | <1 | Insulin secretion defect | Child or adult-onset diabetes | Diet or OAD or insulin |

**Table 1:** Table showing types of MODY and their clinical characteristics [10].

Mutations in the B Lymphocyte Tyrosine Kinase (BLK) locus are very rare. It is an important point that the number of cases with this MODY type, which is defined as BLK 1 mutation, in other words MODY 11, is very low. Borowiec discovered that B Lymphocyte Kinase (BLK) is a previously unknown modulator of insulin production and secretion that increases the expression of critical cell transcription factors PDX-1 and NKX6. [1]. BLK is a non-receptor tyrosine-kinase of the src family of proto-oncogenes. Borowiec et al. reported that mutations in BLK caused diabetes in three families. Bulus et.al from Turkey has reported a case of BLK gene mutation in a 17 year old patient in a case report published in annals of clinical case reports in February 2023 [11]. We present a rare interesting case of 27 years old BLK gene mutation MODY 11 diabetes.

**Case Discussion**

A male person presented with symptoms of easy fatigue with 2 years of duration of diabetes with family history of both parents having diabetes at the age of 40 years. He had 7 siblings out of which 4(3 sisters and one brother) had diabetes at 20 to 30 years. His weight was 79 kilogram, height 169 cms. Informed consent was taken from the patient. This patient was treated at Karnataka institute of endocrinology and research, Bengaluru on 25th March 2026 (Fig. 1).

*Clinical Features*

Duration of diabetes – 2 years.
BMI - 27.66 kg/square meter.
Waist circumference -88 cms.
Pulse -95/minute and
Blood pressure-127/78 mm.
Systemic examination - normal.
Investigations done on 25-3-2026

FPG-212 mg/dl
PPPG-313 mg/dl
HBA1c - 8.8%
Total cholesterol-199 mg/dl
Triglycerides-309 mg/dl
LDL-95 mg/dl
HDL-42 mg/dl
Total Bilirubin 1 mg/dl,
Total protein – 8 gram/dl, albumin-4.4 gram and globulin 3.6 grams
SGOT-64 IU/ml
SGPT-138/ml
GGT-42 IU/L
Alkaline phosphatase -66 IU/L
TSH-2.5 microIU/ML and FT4-1.3 nanogram/dl.
Vitamin D -12 nanogram/ml
Vitamin B12 – 582 picogram/ml.
Serum creatinine-0.77 mg/dl.
Urine microalbuminuria-18.47 mg/gram.
Fasting C-peptide-2.56 nanogram/ml
Stimulated C-peptide-4.63 nanogram/ml
Fundus – normal.
He was treated previously with metformin 1000 mg and sitagliptin 100 mg. Glimepride 1 mg bid was started.
On 28-4-2026 after treatment
FPG-119 mg/dl
PPPG-113 mg/dl

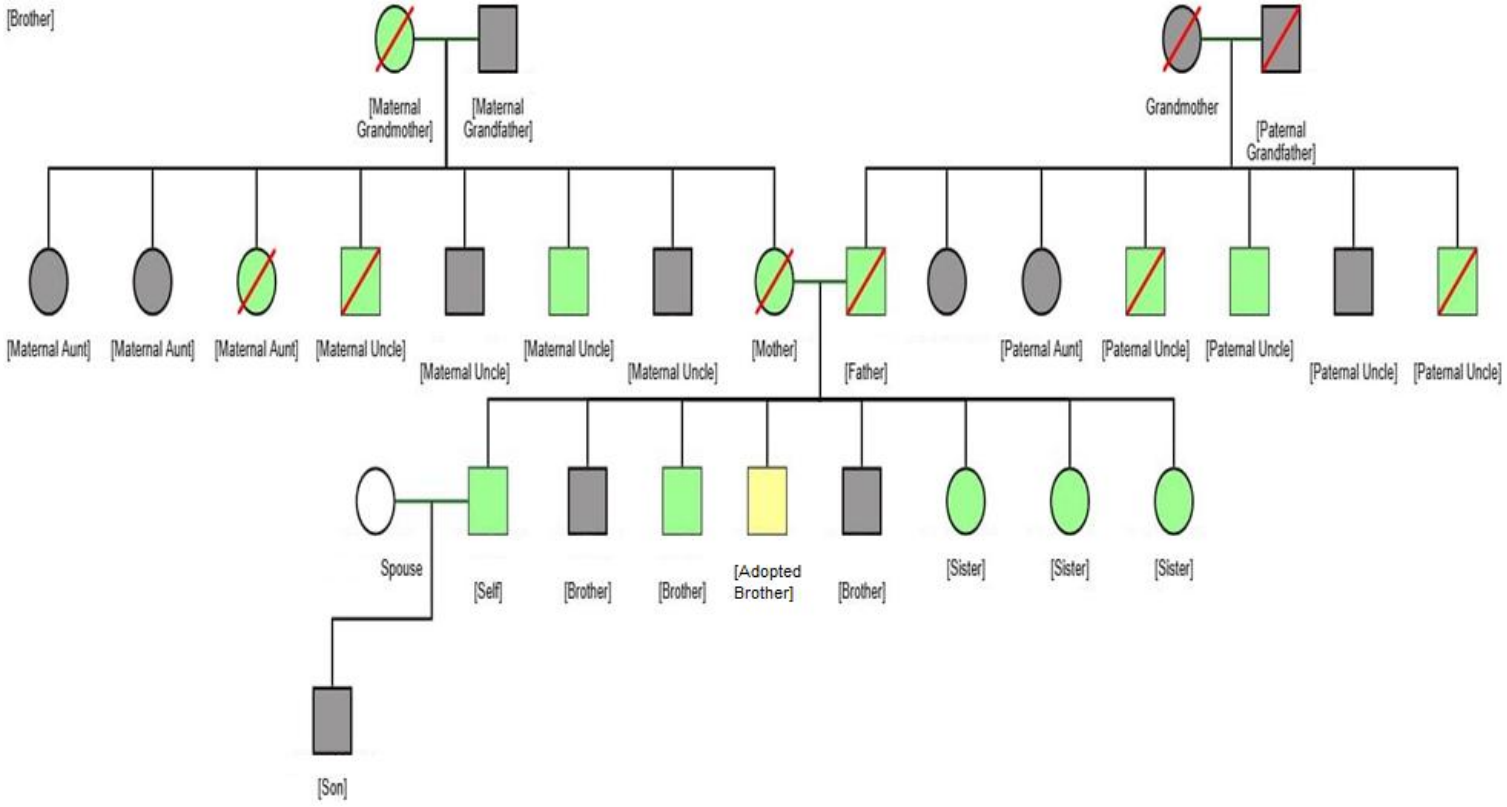


**Figure 1:** Family tree details.

**Methodology**

EDTA-whole blood (2 to 3 ml) was collected and genomic DNA was extracted for NGS library preparation. Library preparation and Exome capture was performed and the enriched library was sequenced on the NGS platform. A 150-bp paired-end run was performed. Probe hybridization-based capture of all coding exons and exon-intron junctions of the targeted genes was employed, followed by Next Generation sequencing. The sequencing reads were assessed for quality and the high-quality reads were aligned to the GRCh38 reference genome. The aligned reads were processed and used for calling Single Nucleotide Variants (SNVs) and small insertions/deletions (indels). The variants are classified and reported as per the ACMG/AMP sequence variant interpretation and reporting guidelines.

Analytical Sensitivity - The analytical sensitivity is approximately 99% for Single Nucleotide Variants (SNVs) and >93% for insertions/duplications/deletions (indels) from 1-10 base pairs in size. Indels greater than 10 base pairs may be detected, but the analytical sensitivity may be reduced. Specificity is >99.9 % for all variant classes.

Whole Exome Sequencing (WES) - is a comprehensive genetic test that examines the exons or protein-coding regions, of the genome, which account for approximately 1-2% of the entire genome but harbour the majority of known disease-causing variants. By focusing on these critical regions, WES enables the identification of genetic changes that may explain clinical symptoms or provide insights into the underlying cause of genetic conditions. This test is particularly valuable for diagnosing rare diseases, complex phenotypes and conditions with heterogeneous genetic causes. The results are interpreted in the context of the patient's clinical and family history, offering insights that can impact patient care and genetic counseling for families. While it primarily targets known coding regions, WES also offers the potential to uncover novel genetic associations, broadening its scope in clinical and research settings. This test aims to identify genetic causes, guiding personalized care, early interventions and family-centered management strategies.

*Genetic Analysis Report*

The 27-year-old male patient presented for evaluation to rule out Maturity-Onset Diabetes of the Young (MODY).

**Results**

*Report Summary*

Result: Detected (Table 2)

| Gene | Variant | Zygosity | Inheritance | Disease | Variant Classification |
|---|---|---|---|---|---|
| *BLK* | NM_001715.3(BLK): c.1267G>C(p.Val423Leu) | Heterozygous* | Autosomal dominant | Maturity-onset diabetes of the young, type 11 | Variant of Uncertain Significance (VUS) (PM2) |

**Table 2:** Results of the patient gene evaluation.

*Interpretation*

BLK: A heterozygous variant of uncertain significance NM_ 001715.3(BLK): c.1267G>C (p.Val423Leu) in exon 12 of the BLK gene (chr8:11563065 G>C; Depth: 250x; VAF:53.60%) was identified in the given sample. Missense mutations in the gene are known to be associated with Maturity-onset diabetes of the young (MODY) (PMID: 35108381). The variant is absent from the 1000 Genomes databases and ExAC database and has a minor allele frequency of 0.0001% in gnome AD database. The heterozygous variant in BLK gene identified is classified as a VUS (PM2 only). Maturity-onset diabetes of the young, type 11: Maturity-onset diabetes of the young (MODY11) is caused by heterozygous mutation in the BLK gene on chromosome 8p23-p22. MODY (maturity-onset diabetes of the young) is a rare, familial, clinically and genetically heterogeneous form of diabetes characterized by young age of onset (generally 10-45 years of age) with maintenance of endogenous insulin production, lack of pancreatic beta-cell autoimmunity, absence of obesity and insulin resistance and extra-pancreatic manifestations in some subtypes (OMIM:613375, ORPHA:552). Genetic counseling is recommended. Parental segregation analysis is recommended to aid in the reclassification of the identified Variant of Uncertain Significance (VUS).

**Discussion**

MODY 11 is an extremely rare form of monogenic diabetes caused by mutations in the BLK (B-lymphocyte kinase) gene. It typically manifests as non-insulin-dependent diabetes with an early onset. Borowiec re-sequenced 732 kb of genomic sequence at 8p23 in 6 MODY families unlinked to known MODY genes that showed evidence of linkage at that location. Of the 410 sequence differences that we identified, 5 had a frequency <1% in the general population and segregated with diabetes in 3 of the families, including the 2 showing the strongest support for linkage at this location. The 5 mutations were all placed within 100 kb corresponding to the BLK gene. One resulted in an Ala71Thr substitution; the other 4 were noncoding and determined decreased in vitro promoter activity in reporter gene experiments. We found that BLK--a nonreceptor tyrosine-kinase of the src family of proto-oncogenesis Expressed in beta-cells where it enhances insulin synthesis and secretion in response to glucose by up-regulating transcription factors Pdx1 and Nkx6.1. These actions are greatly attenuated by the Ala71Thr mutation. These findings point to BLK as a previously unrecognized modulator of beta-cell function, the deficit of which may lead to the development of diabetes [12].

Kim, et al., initially mapped this locus on chromosome 8p23 by a genome wide scan of 21 extended United States families segregating autosomal dominant MODY not caused by known MODY genes [13]. They noted that there was a higher prevalence of obesity in individuals with diabetes that was linked to 8p23 than in diabetic individuals with MODY linked to other loci (Fig. 2).

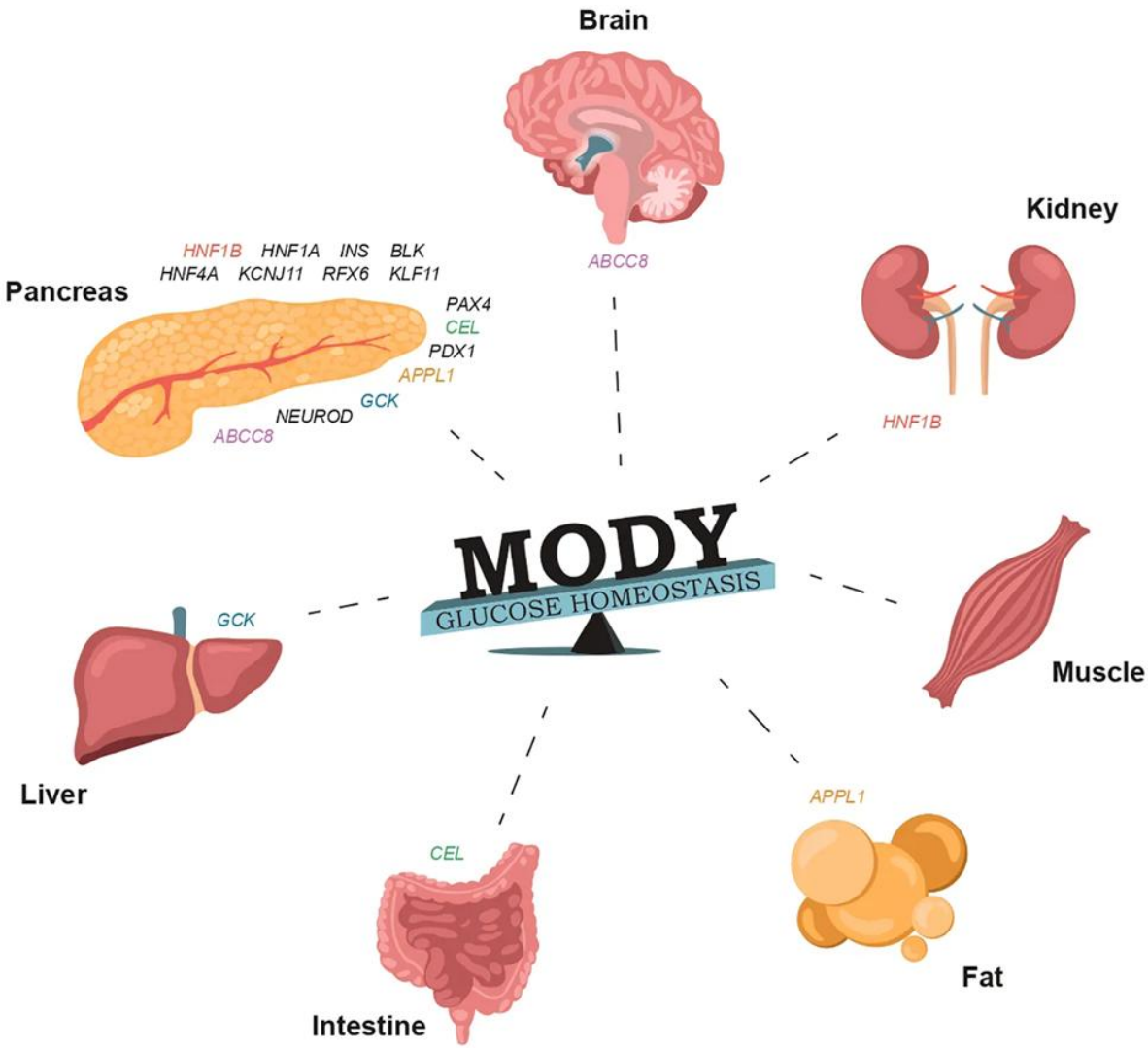


**Figure 2:** The involvement of specific genes in glucose homeostasis and the normal functioning of organs that regulate carbohydrate and lipid metabolism can result in damage that may manifest in various forms of MODY [14].

*Clinical Characteristics of MODY 11 with BLK Gene Mutation*

Unlike many other forms of MODY which are often associated with leanness, MODY 11 has a notable association with higher body mass. Diabetes usually develops in adolescence or early adulthood, typically before the age of 25-30. The condition is driven by impaired insulin secretion due to defects in the BLK protein, which is necessary for normal insulin synthesis and secretion in pancreatic beta-cells. It follows a strong familial pattern where one copy of the mutated gene is enough to cause the disorder, often spanning three or more generations. Patient's lack the pancreatic autoantibodies such as GAD typically found in Type 1 diabetes. Evidence of endogenous insulin production persists, measured by detectable C-peptide levels even years after diagnosis. Despite high blood sugar, patients rarely experience severe Diabetic Ketoacidosis (DKA) at the time of diagnosis [15]. Treatment for MODY 11 is highly individualized and may require a combination of therapies. Many patients initially respond to oral sulfonylureas or other Oral Hypoglycemic Agents (OHAs). In some cases, oral medications alone are insufficient for glycemic control, requiring the addition of basal insulin. Weight management is a critical component of treatment due to the higher prevalence of obesity in this specific subtype (Table 3).

| | | |
|---|---|---|
| 1 | BMI | 27.66 |
| 2 | Waist circumference | 88 cms |
| 3 | Age of onset of diabetes | 25 years |
| 4 | Family history | Positive in 3 generations |
| 5 | Ketosis | Absence of ketosis |
| 6 | Inheritance | Autosomal dominant |
| 7 | Fasting C-peptide | 2.56 nanogram/ml |
| 8 | Stimulated C-peptide | 4.63 nanogram/ml |
| 9 | Response to OHA | Good |

**Table 3:** Clinical features of present case which fit into MODY11.

**Conclusion**

This is a case of BLK gene heterozygous mutation MODY 11, male aged 27 years with obesity, age of onset of diabetes at 25 years, autosomal dominant inheritance with strong family history of diabetes in three generations with evidence of endogenous insulin production and absence of ketosis. He responded well to treatment with oral drugs.

**Conflict of Interest**

The authors declared no potential conflicts of interest with respect to the research, authorship and/or publication of this article.

**Funding Statement**

This research did not receive any specific grant from funding agencies in the public, commercial or non-profit sectors.

**Acknowledgement**

The authors have no acknowledgments to declare.

**Data Availability Statement**

The data supporting the findings of this study are available from the corresponding author upon reasonable request.

**Ethical Statement**

The project did not meet the definition of human subject research under the purview of the IRB according to federal regulations and therefore was exempt.

**Informed Consent Statement**

Informed consent was obtained from all participants included in the study.

**Authors' Contributions**

All authors contributed equally to this paper.

**References**


1. Anık A, Çatlı G, Abacı A, Böber E. Maturity-onset diabetes of the young (MODY): An update. J Pediatr Endocrinol Metab. 2015;28(3-4):251-63.
2. Tattersall RB, Fajans SS. A difference between the inheritance of classical juvenile-onset and maturity-onset type diabetes of young people. Diabetes. 1975;18:44-53.
3. Froguel P, Vaxillaire M, Sun F. Close linkage of glucokinase locus on chromosome 7p to early-onset non-insulin-dependent diabetes mellitus. Nature. 1992;356:162-4.
4. Hoffman LS, Jialal I. Diabetes, maturity onset in the young (MODY). In: StatPearls. Treasure Island (FL): StatPearls Publishing. 2020.
5. Henzen C. Monogenic diabetes mellitus due to defects in insulin secretion. Swiss Med Wkly. 2012;142:w13690.
6. Delvecchio M, Pastore C, Giordano P. Treatment options for MODY patients: A systematic review of literature. Diabetes Ther. 2020;11(8):1667-85.
7. Kleinberger JW, Pollin TI. Undiagnosed MODY: Time for action. Curr Diab Rep. 2015;15:110.
8. Kanthimathi S, Balamurugan K, Mohan V. Identification and molecular characterization of HNF1B gene mutations in Indian diabetic patients with renal abnormalities. Ann Hum Genet. 2015;79:10-9.
9. Mohan V, Unnikrishnan R, Radha V. Exciting discovery of a new maturity-onset diabetes of the young subtype from India (MODY 15). J Assoc Physicians India. 2025;73(7):11-3.
10. Urakami T. Maturity-onset diabetes of the young (MODY): Current perspectives on diagnosis and treatment. Diabetes Metab Syndr Obes. 2019;12:1047-1056.
11. Bulus AD, Yasartekin Y, Ortlek H, Ceylan AC. BLK-1 mutation with maturity onset diabetes of the young 11: A case report. Ann Clin Case Rep. 2023;8:2385.
12. Borowiec M, Liew CW, Thompson R, Boonyasrisawat W, Hu J, Mlynarski WM, et al. Mutations at the BLK locus linked to maturity onset diabetes of the young and beta-cell dysfunction. Proc Natl Acad Sci U S A. 2009;106(34):14460-5.
13. Kim SH, Ma X, Weremowicz S, Ercolino T, Powers C, Mlynarski W, et al. Identification of a locus for maturity-onset diabetes of the young on chromosome 8p23. Diabetes. 2004;53:1375-84.
14. Dzhemileva LU, Zakharova EN, Goncharenko AO, Vorontsova MV, Rumyantsev SA, Mokrysheva NG, et al. Current views on etiology, diagnosis, epidemiology and gene therapy of maturity onset diabetes in the young. Front Endocrinol. 2025;15:1497298.
15. Aarthy R, Aston-Mourney K, Amutha A, Mikocka-Walus A, Anjana RM, Unnikrishnan R, et al. Prevalence, clinical features and complications of common forms of Maturity Onset Diabetes of the Young (MODY) seen at a tertiary diabetes centre in South India. Prim Care Diabetes. 2023;17(4):401-7.