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ABCC8 Gene Factors in Maturity-Onset Diabetes of The Young (MODY): Literature Review

Tri Setyawati[1]*, Ryka Marina Walanda[2], Intania Rieska Putri[2], Devi Oktaviani[2], Sulisda[2]

[1] Departement of Biochemistry, Faculty of Medicine, Tadulako University, Palu, Indonesia
[2] Student of Medical Profession, Faculty of Medicine, Tadulako University, Palu, Indonesia

Corresponding Author Email: tridentist@gmail.com

LITERATURE REVIEW

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ABSTRACT

Maturity-Onset Diabetes of the Young (MODY) is a monogenic form of diabetes characterized by single-gene mutations affecting insulin secretion, typically manifesting in young individuals. Mutations in the ABCC8 gene (MODY12), encoding the SUR1 subunit of the pancreatic β-cell K-ATP channel, are a recognized, albeit relatively rare (1-3% prevalence), cause. This literature review aimed to summarize cases of ABCC8-MODY, detailing genetic and clinical features, differentiating it from Type 1 (T1DM) and Type 2 (T2DM) diabetes, and outlining treatment strategies. A systematic literature search was conducted in Google Scholar (2020-2024) using the keywords "ABCC8 gene," "diabetes," and "young age." From an initial pool of 1,010 articles, a rigorous screening process based on predefined inclusion and exclusion criteria yielded 7 relevant studies. The ABCC8 gene plays a critical role in insulin secretion through the K-ATP channel; mutations result in β-cell dysfunction and MODY12, exhibiting variable phenotypes. Misdiagnosis as T1DM or T2DM is common. Key diagnostic features of MODY include young age of onset (<25-35 years), a strong family history, absence of pancreatic autoantibodies, detectable endogenous insulin production (C-peptide), and often, high sensitivity to sulfonylureas (SUs). Accurate diagnosis necessitates a thorough clinical history, physical examination, and definitive molecular genetic testing, such as next-generation sequencing (NGS). Notably, patients with ABCC8-MODY typically demonstrate a favorable response to SU therapy, underscoring the importance of early and accurate diagnosis for optimal management.

Key Messages:

- MODY, particularly resulting from ABCC8 gene mutations, is often misdiagnosed as Type 1 or Type 2 diabetes, highlighting the need for increased clinical suspicion in cases of young-onset diabetes
- Patients with ABCC8-MODY often exhibit high sensitivity to sulfonylureas (SUs), making SUs the recommended first-line treatment, distinct from management strategies for T1DM or T2DM

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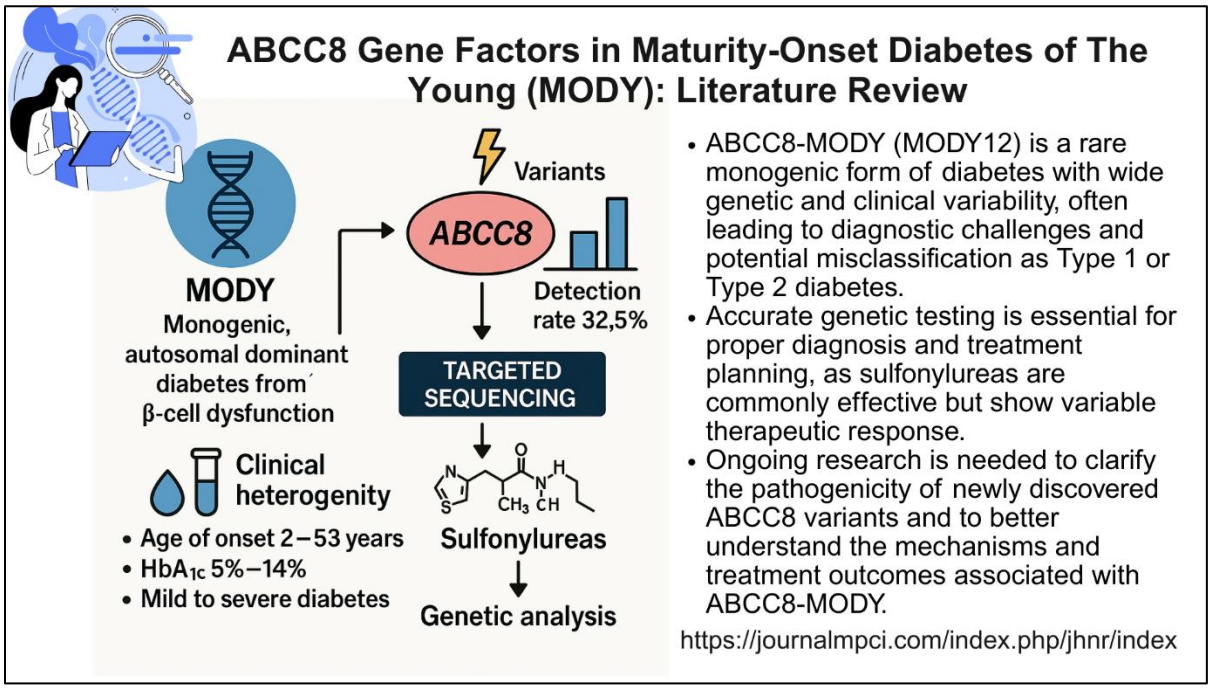
GRAPHICAL ABSTRACT



INTRODUCTION

Maturity-onset diabetes of the young (MODY) is diabetes mellitus that occurs in young people. This diabetes is a monogenic form of diabetes mellitus in which one gene codes for insulin secretion. Generally caused by genetic defects related to dysfunction of pancreatic β-cell secretion. Maturity-onset diabetes of the young is a rare condition, accounting for 1-5% of all diabetes cases and is easily misdiagnosed as type 1 (T1DM) or type 2 (T2DM) diabetes mellitus in clinical practice. One study showed that 80% of diabetes cases in young people were initially misdiagnosed as type 1 or type 2 diabetes (1,2).

The discovery of the gene that codes for insulin secretion to date contains 14 subtypes. The genetic etiology that induces diabetes at a young age (MODY) that has been identified is GCK, HNF1A, HNF4A, HNF1B, PDX1, NEUROD1, KLF11, CEL, PAX4, INS, BLK, KCNJ11, ABCC8 (binding cassette transporter subfamily C member 8) and APPL1 (1).

Mutations in the ABCC8 gene have a low prevalence among juvenile diabetes subtypes. The figure only accounts for around 1% - 3% of all diabetes in young people. According to several studies, the prevalence of MODY due to ABCC8 mutations ranges from 0.9 to 3.3% among clinically suspected MODY cohorts, possibly equivalent to 30–50 cases per 1,000,000 people (3).

In juvenile diabetes mellitus, either type 1 or type 2 (MODY12), pathogenic mutations can be found in the ATP-binding cassette transporter subfamily C member 8 (ABCC8) gene, which is located on chromosome 11. This gene subfamily encodes sulfonylurea receptor 1 (SUR1). The SUR1 gene plays a role in regulating potassium channels in pancreatic beta cells (4). In autosomal dominant inheritance of diabetes mellitus, there are several phenotypes that can appear. In people with a history of diabetes in at least three generations, clinical findings are positive before the age of 25 years (5).

The ATP-sensitive potassium channel (K-ATPase) in β cells consists of two subunits, namely the subunit encoded by the Potassium Inwardly Rectifying Channel Subfamily J Member 11 (KCNJ11) gene and the regulatory gene subunit encoded by the ABCC8 gene. Insulin secretion is mediated by the closure of these K channels by ATP binding, so that mutations in either gene affect insulin secretion. The ABCC8 gene consists of 39 exons coding for 1582 amino acids. Several types and locations of ABCC8 gene mutations have been reported (4). This literature review aims to systematically review reported cases of *ABCC8*-MODY, detailing its genetic and clinical features, distinguishing characteristics from T1DM and T2DM, and exploring optimal treatment strategies. Accurate and timely diagnosis of *ABCC8*-MODY is crucial due to the

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high sensitivity of these patients to sulfonylurea (SU) therapy. Misdiagnosis and inappropriate management can lead to significant morbidity and mortality. Therefore, there is a clinical urgency to identify *ABCC8*-MODY early, facilitating appropriate treatment and preventing complications. Identifying genetic defects underlying MODY, particularly *ABCC8* mutations, is paramount for distinguishing MODY from other diabetes types and optimizing patient care based on specific underlying pathophysiology and therapeutic responsiveness (5).

Key diagnostic features of MODY include young age of onset (typically <25 years), a strong family history of diabetes spanning multiple generations, absence of pancreatic autoantibodies, detectable endogenous insulin production (C-peptide), and often, a favorable response to low-dose sulfonylureas. Definitive diagnosis requires molecular genetic testing, such as next-generation sequencing (NGS). To systematically review reported cases of ABCC8-MODY, detailing its genetic and clinical features, distinguishing characteristics from T1DM and T2DM, and exploring optimal treatment strategies.

METHODS

This study employed a systematic literature review methodology to identify, evaluate, and synthesize relevant research on the *ABCC8* gene's role in Maturity-Onset Diabetes of the Young (MODY). A comprehensive search was conducted using Google Scholar as the primary database, utilizing the keywords "ABCC8 gene," "diabetes," and "young age." The search was limited to publications within the last five years (2020-2024) to ensure the inclusion of contemporary research.

Justification for Google Scholar

While acknowledging the limitations of Google Scholar compared to specialized databases such as PubMed or Scopus, its broad coverage of multidisciplinary literature, including journals and grey literature, was deemed suitable for this initial scoping review. Future studies may benefit from utilizing more specialized databases to enhance comprehensiveness. Inclusion criteria: Articles were included if they focused on the *ABCC8* gene's role in diabetes presenting at a young age and were published between 2020 and 2024. Exclusion criteria**:** Articles were excluded if they only provided abstracts without full-text access or discussed MODY without specific reference to the *ABCC8* gene.

Screening and Selection Process

Initially, titles and abstracts were screened to identify potentially relevant articles. Subsequently, full-text articles were retrieved and assessed for eligibility based on the predefined inclusion and exclusion criteria. Two independent reviewers evaluated each article to minimize bias during the screening and selection process. Discrepancies were resolved through discussion and consensus.

Data Synthesis

A narrative synthesis approach was used to analyze and synthesize the data extracted from the included studies. Thematic analysis was employed to identify, analyze, and report patterns (themes) within the data. This involved iteratively coding and categorizing information related to the genetic and clinical features of *ABCC8*-MODY, its differentiation from T1DM and T2DM, and treatment strategies.

RESULTS

In the initial stage of the literature search, 1,010 journal articles were obtained using the keywords "ABCC8 gene, diabetes, and young age". Next, screening was carried out on the titles and abstracts of the articles so that 35 articles remained due to inappropriate discussion topics. Then, an analysis was carried out on the remaining articles. Articles that fell within the exclusion criteria and had similar content to other articles were excluded, so the final total of articles to be reviewed was 7.

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Table 1. Summary of Studies Analyzing Genetic Variants in MODY

No	Author	Year	Title	Method and sample	Review
1	Hamide Betül Gerik celebi, Meliha Demiral (6)	2023	Evaluation of variants in maturity onset of diabetes young related genes in Balıkesir region	In a case study using data from May 2018 to April 2023, 40 pediatric patients (n=25 females, n=15 males) with a clinical diagnosis of MODY were evaluated by targeted genome sequencing.	• Through targeted genome sequencing analysis, genetic diagnostics detected results in 32.5% (13/40) of MODY patients. • The MODY12 subtype is this study's second most commonly found subtype. When evaluated, GCK mutations were the most common variant in all age groups in the study region. • The ABCC8 gene mutation was the second most common mutation in the study. • The ABCC8 gene variant is involved in about 1% of MODY cases.
2	Leweihua Lin, Huibiao Quan, Kaining Chen, Daoxiong Chen, Danhong Lin and Tuanyu Fang, (7)	2020	*ABCC8*-Related Maturity-Onset Diabetes of the Young (MODY12): A Report of a Chinese Family	A case study was conducted on families in China who have a family history of diabetes for three generations. A total of nine people have been diagnosed with diabetes or glucose tolerance disorder, three of whom were diagnosed before the age of 45, and the earliest diagnosed age was 12 years. Then genetic analysis was carried out on the research sample.	• Diabetes mellitus at a young age (MODY) is a monogenic diabetes characterized by autosomal dominant inheritance. • Its atypical clinical picture makes diagnosis difficult and can be misdiagnosed as type 1 or type 2 diabetes. • Fourteen MODY subtypes have been diagnosed so far, of which MODY12 is caused by a mutation of the ABCC8 (ATP Binding Cassette Subfamily C Member 8) gene, which is rarely reported in China. • This article reports on a case of MODY12 caused by a single nucleotide mutation

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No	Author	Year	Title	Method and sample	Review
					from cytosine to thymine at the 4,544 position of the ABCC8 gene. • This mutation has not been reported to be associated with MODY in China or other countries. This is a rare mutation of the ABCC8 missense gene.
3	Chaoyan Tang, Liheng Meng, Ping Zhang, Xinghuan Liang, Chaozhi Dang, Hui Liang, Junfeng Wu, Haiyun Lan and Yingfen Qin (8)	2021	Case Report: A Novel ABCC8 Variant in a Chinese Pedigree of Maturity-Onset Diabetes of the Young	The study used a sample of a Chinese family suspected to be MODY, a 15-year-old female patient with diabetes. Clinical data and blood samples were collected from probandus and other family members. All surviving relatives were given an oral glucose tolerance test. The next generation sequence is performed to identify the mutated genes in the probandus.	• This study revealed a new missense variant of the ABCC8 gene in a Chinese family. • These findings suggest that these family members respond to treatment with sulfonylurea, as seen earlier in ABCC8 MODY.
4	Karunakaran, Wei, and Bano (9)	2020	Monogenic Diabetes due to ABCC8/ KCNJ11 Mutation: Case Study and Review of Literature	This article presents a 58-year-old woman with diabetes who was detected with the ABCC8 mutation during cascade testing. He was diagnosed with diabetes at the age of 12. Her son had a history of neonatal hypoglycemia and had diabetes at the age of 15.	• Monogenic diabetes is classified into three main groups: neonatal diabetes, which mostly appears in the first six months of birth; diabetes onset maturity at a young age (MODY); and maternal inherited mitochondrial diabetes. • Mutations in the ABCC8/KCNJ11 gene also cause monogenic diabetes. Mutations of this gene are found in ~50% of patients with congenital hyperinsulinemia (CHI). • In these cases, diabetes usually appears in the neonatal period (temporary or permanent) or in adolescence/early adulthood.

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No	Author	Year	Title	Method and sample	Review
5	Daniel Zamanfar, Seyed Mohammad Bagher Hashemi-Soteh, Mobin Ghazaiean and Mahsa Amoli (10)	2022	Report of a Novel Mutation of ABCC8 Gene Related to MODY12 Phenotype	Case studies of the clinical picture, ABBC8 mutations, and related findings in 2.5-year-old boys (currently 8 years old) were referred to clinics with complaints of polydipsia, polyuria, polyphagia and weight loss unrelated to ketoacidosis.	• Monogenic diabetes mellitus includes many different types of diabetes. • The most common type is Maturity-onset diabetes of the young (MODY). • The ABCC8 gene is one of the genes that plays an important role in the function of the K-ATP channel and its mutations cause various types of diabetes with different manifestations. • Different symptoms make diagnosis difficult, which has a direct impact on patient management. • A single nucleotide mutation in the case of MODY12 shows the replacement of the amino acid phenylalanine with tyrosine in nucleotide #368, which has not been reported recently.
6	Marijke Timmers, Eveline Dirinck, Patrick Lauwers, Wim Wuyts, Christophe De Block (4)	2021	ABCC8 variants in MODY12: Review of the literature and report of a case with severe complications	This article conducted a structured search on Google Scholar, PubMed, the National Center for Biotechnology Information for specific mutations of the presented cases and other ABCC8 genetic variants that cause MODY12. Based on the ABCC8 genetic variant reported in the mastermind.genomenon.com database, this article includes all relevant papers published in English up to November 15, 2020.	• More than 1000 variants of ATP-binding cassette transporter subfamily C member 8 (ABCC8) have been reported in neonatal diabetes mellitus. • To date, only 55 ABCC8 variants have been associated with Maturity-Onset Diabetes of the Young 12 (MODY12). • This article presents the c.3544C>T p.(Arg1182Trp) ABCC8 variant in a 35-year-old woman with complications

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No	Author	Year	Title	Method and sample	Review
					of microvascular diabetes and charcot arthropathy that require lower extremity amputation. • The current mutation is mostly associated with neonatal diabetes and only three papers report MODY12. • The 55 MODY12 variants showed great clinical heterogeneity, even in relatives with the same mutation, ranging from mild glucose tolerance disorders to severe insulin-dependent diabetes mellitus. • HbA1c at diagnosis ranges from 5% to 14% and age at diagnosis ranges from 2 to 53 years.
7	Marella Marassi, Mario Luca Morieri, Viola Sanga, Giulio Ceolotto. Angelo Avogaro, Gian Paolo (3)	2024	The Elusive Nature of ABCC8-related Maturity-Onset Diabetes of the Young (ABCC8-MODY). A Review of the Literature and Case Discussion	This article illustrates three case reports that are suspected of having an ABCC8-MODY diagnosis after the identification of a new variant of ABCC8 of unknown significance. This article discusses that careful interpretation of genetic testing is necessary even against the background of a suggestive clinical context.	• Maturity-onset diabetes of the young (MODY) is a monogenic form of diabetes caused by a genetic defect, usually autosomal dominant transmitted, that causes β cell dysfunction. • Fourteen subtypes of MODY have been described to date. The Latest Findings of ABCC8-MODY are caused by a mutation in the cassette carrier gene of the C-member subfamily 8 (ABCC8) that binds adenosine triphosphate (ATP), which is involved in regulating insulin secretion. • The complexity of the ABCC8-MODY genetic picture is

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No	Author	Year	Title	Method and sample	Review
					reflected by its diverse clinical manifestations, covering a broad spectrum of disease severity. Correct diagnosis is essential for choosing an adequate treatment and improving outcomes. By targeting damaged gene products, sulfonylurea is the drug of choice in ABCC8-MODY, although its efficacy varies widely. • The article highlights the need for further research to uncover the mechanisms of ABCC8-MODY disease, as well as to clarify the pathogenicity of the identified ABCC8 variants and their responses to therapy.

The reviewed studies collectively investigate the genetic landscape of Maturity-Onset Diabetes of the Young (MODY), with a significant focus on variants within the ABCC8 gene, which cause the MODY12 subtype. MODY is established as a monogenic, autosomal dominant form of diabetes stemming from β-cell dysfunction, presenting diagnostic challenges due to its clinical heterogeneity. Genetic analysis, particularly targeted sequencing, is essential for accurate diagnosis, although detection rates can vary, as seen in the Turkish study identifying causative variants in 32.5% of their cohort. While GCK mutations were most common in that specific region, the ABCC8 variant emerged as the second most frequent, contrasting with general estimates suggesting ABCC8 accounts for only about 1% of MODY cases globally and is reported rarely in some populations like China. Several studies highlight the discovery of novel ABCC8 missense mutations associated with MODY12 in different populations (Chinese families and Iranian individuals), underscoring the ongoing identification of new genetic contributors (Table 1).

The clinical spectrum associated with ABCC8-MODY is remarkably diverse, as emphasized across multiple reports. Phenotypes range from mild glucose tolerance impairment to severe, insulin-dependent diabetes, sometimes accompanied by significant complications like microvascular issues and Charcot arthropathy. This heterogeneity exists even among individuals sharing the same mutation, with age of onset varying widely (from 2 to 53 years) and diagnostic HbA1c levels spanning from 5% to 14%. This variability complicates diagnosis, potentially leading to misclassification of Type 1 or Type 2 diabetes. Accurate genetic diagnosis is crucial as it informs treatment strategies, with sulfonylureas being the typical therapy for ABCC8-MODY by targeting the defective gene product, although treatment efficacy shows considerable variation. The studies stress the need for careful interpretation of genetic results, especially for variants of unknown significance, and call for further research to fully elucidate disease mechanisms, variant pathogenicity, and therapeutic responses in ABCC8-MODY (Table 1).

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DISCUSSION

Monogenic diabetes refers to the type of diabetes that results from monogenic mutations, with the most common type being diabetes of the young (MODY) (7). Monogenic diabetes is usually misdiagnosed as type 1 or type 2 diabetes mellitus (DM) because the clinical features are similar. However, the treatment strategy and prognosis are different from other types of DM (8). Over the past two decades, the number of genetic mutations and various forms of MODY has increased from the initial description of 6 subtypes to 14 subtypes (11). However, based on the latest revision of gene-disease associations, the list of MODY causative genes Current Diabetes Reports (2024) 24:197 –206 should be restricted to HNF4A, GCK, HNF1A, PDX1, HNF1B, NEUROD1, CEL, INS, ABCC8, KCNJ11, along with RFX6, which has recently been proposed as an additional MODY gene (3).

Mechanisms involved in MODY pathogenesis include defective transcriptional regulation, abnormal metabolic enzymes, protein misfolding, dysfunctional ion channels, or impaired signal transduction (12). The ABCC8 gene can cause various beta cell dysfunctions, including MODY. The ABCC8 gene is located on chromosome 11p15 and encodes the sulfonylurea receptor 1 (SUR1) subunit of the ATP-sensitive potassium channel (KATP) in pancreatic β cells, which is involved in the electrical activity of the plasma membrane, thereby regulating insulin secretion. ABCC8 gene mutations can cause various phenotypes, resulting in overactive or underactive KATP channels, resulting in abnormal glucose metabolism (10).

Recessive loss-of-function mutations in ABCC8 cause the development of congenital hyperinsulinism and hypoglycemia (CHI), whereas dominantly inherited ABCC8 mutations can cause CHI with a predisposition to insulin deficiency and diabetes later in life. Heterozygous activating mutations in ABCC8 cause MODY without a history of diabetes or hyperinsulinism in the neonatal period, and produce clinical manifestations similar to those of HNF1A/4A MODY (13).

In 2012, Bowman et al. first reported that MODY12 is caused by mutations in the ABCC gene with its variable clinical manifestations, possibly related to body weight and usually without significant hypertriglyceridemia and hypercholesterolemia. Furthermore, the family may also have a history of neonatal diabetes (10).

The atypical clinical picture of MODY is the main cause of misdiagnosis. The clinical characteristics of MODY are a history of MODY monogenic diabetes in the family, diabetes that appears early in adolescence or young adulthood (generally at age <35 years but <25 years likely to be higher in MODY criteria), extreme sensitivity to sulfonylureas, history of neonatal diabetes or neonatal hypoglycemia. evidence of endogenous insulin production beyond the “honeymoon” or remission phase (more than 3-5 years after diabetes diagnosis) with detectable C-peptide (>0.6 ng/mL or >0.2 nmol/L) when glucose > 72 mg/dL or >4 mmol/L) which will persist (more than 3-5 years (14).

The clinical feature differentiating MODY from type 1 diabetes mellitus is the absence of pancreatic antibodies, especially when measured during diagnosis. At that time, insulin requirements are low for treatment, for example, <0.5 U/kg/day. Apart from that, there was no ketoacidosis in MODY when insulin was removed from treatment. Clinical features that can differentiate MODY from type 2 diabetes mellitus are the onset of diabetes before the age of 45 years with a normal body mass index, absence of acanthosis nigricans, normal triglyceride levels, and/or normal or increased high-density lipoprotein cholesterol (HDL-C) seen in HNF1A -MODY(12) Although MODY shares some clinical similarities with type 2 diabetes, the low-grade inflammatory processes seen in type 2 diabetes, obesity, and cardiovascular disease do not play a role in the pathophysiology MODY (15).

A family history of 3 generations (or more) should be obtained when taking anamnesis of the patient and family members and through medical records whenever possible. Things that need to be considered are the age at the onset of diabetes mellitus, body habits at the onset of diabetes, insulin independence, medication used, hypoglycemia, and molecular genetic testing. (12) Independence or not requiring insulin or requiring low doses (<0.5 U /kg), and good metabolic control are appropriate steps in the diagnosis of diabetes mellitus at a young age.

Having polygenic diabetes may result in a missed diagnosis of MODY because the patient may not meet the criteria for genetic testing. The mutation is most likely detected only when a relative shows the

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MODY phenotype and is referred for genetic testing. The specificity of BMI for differentiating type 2 diabetes from MODY will decrease as the prevalence of obesity increases, and BMI cutoffs in MODY testing eligibility criteria will need to be relaxed or eliminated altogether to prevent misdiagnosis (16).

Molecular genetic testing is essential for appropriate treatment and genetic counseling. Based on a systematic review, Genetic testing can be performed with Next Generation Sequencing (NGS) (6). However, specific criteria must be met to ensure an accurate diagnosis before performing genetic testing. (17). At the clinical findings stage, the clinical phenotype of the ABCC8 (MODY 12) gene may vary depending on the type and location of the mutation, as has been discovered. Clinical manifestations may begin at any age, including infancy with hyperinsulinemic hypoglycemia or neonatal DM and childhood or adulthood with overt DM (18). Next-generation sequencing (NGS) is most commonly used to identify gene variants involved in MODY and to identify single nucleotide variants (SNVs) (19,20).

Patients with ABCC8 were found to be very sensitive to sulfonylurea (SU) drug therapy. Therefore, since its discovery it has been recommended as a first-line treatment for the ABCC8 gene. Early identification with a detailed history, especially family history and multilevel genetic testing, these patients can receive appropriate follow-up with prompt intervention and treatment when clinically indicated (15,9).

Early identification of ABCC8-MODY through meticulous family history and genetic testing can prevent long-term complications and improve patient quality of life. Furthermore, these findings underscore the need for heightened awareness among clinicians regarding the variability of MODY presentation and the importance of genetic considerations in diagnosing young-onset diabetes. Future research should prioritize the development of evidence-based guidelines for genetic testing and ABCC8-MODY management, as well as exploring alternative therapies for patients' intolerance to sulfonylureas. Thus, this review serves as a valuable resource for clinicians, researchers, and patients in enhancing the understanding and management of ABCC8-MODY

Although this review provides a comprehensive overview of ABCC8-MODY, several limitations must be acknowledged. Firstly, using Google Scholar as the primary search database may introduce certain biases. Despite its broad coverage, Google Scholar lacks the curation and specificity of specialized databases such as PubMed or Scopus, potentially leading to the omission of relevant studies or the inclusion of studies with varying quality. Additionally, the number of studies included in this review is relatively tiny (n=7), which may limit the ability to draw robust generalizations. Secondly, the geographical diversity of the included studies may be under representative. Most studies originated from specific geographical regions, potentially limiting the applicability of the findings to broader and more diverse populations. Genetic variations and environmental factors can influence the clinical presentation and treatment response of ABCC8-MODY, and the lack of geographical diversity may hinder the ability to capture these variations. Therefore, future research should incorporate studies from diverse geographical regions to enhance the generalizability of the findings. Furthermore, more specialized databases and comprehensive search strategies may help mitigate bias and increase the number of studies included.

CONCLUSION

Maturity-Onset Diabetes of the Young (MODY) represents a form of monogenic diabetes mellitus characterized by early-onset hyperglycemia resulting from genetic defects that impair pancreatic β-cell secretion. Among the implicated genetic factors, the *ABCC8* gene plays a crucial role in the function of the K-ATP channel. Mutations within this gene lead to diverse diabetes phenotypes with varying clinical manifestations, underscoring its significant impact on MODY pathogenesis. This review aligns with existing findings, reinforcing the critical role of *ABCC8* in MODY and highlighting its mutations' diagnostic and therapeutic implications.

Future research should focus on several key areas to advance our understanding and management of ABCC8-MODY. Firstly, more extensive cohort studies are needed to elucidate the full spectrum of *ABCC8* mutations and their associated clinical phenotypes across diverse populations. Secondly, functional studies of *ABCC8* mutations are essential to unravel the precise mechanisms by which these genetic variations disrupt K-ATP channel function and contribute to β-cell dysfunction. Finally, developing personalized treatment strategies based on specific *ABCC8* mutations and patient characteristics should be prioritized

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to optimize clinical outcomes and improve the quality of life for individuals with *ABCC8*-MODY.

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CONFLICTS OF INTEREST

The authors declare no conflict of interest.

REFERENCES

1. Sağsak E, Önder A, Peltek Kendirci HN, Yıldız M, Akgün Doğan Ö. Evaluation and Long-term Monitoring of Patients with MODY, and Description of Novel Mutations. jarem. 2022 Aug 25;12(2):99–107.
2. Duzkale N, Emiroglu C. Investigation of the Mutation Spectrum in Pediatric Patients with Maturity-Onset Diabetes of Youth (MODY): Experience from a Diagnostic Center in Türkiye. CD. 2023 Aug 26;12(4):232–8.
3. Marassi M, Morieri ML, Sanga V, Ceolotto G, Avogaro A, Fadini GP. The Elusive Nature of ABCC8-related Maturity-Onset Diabetes of the Young (ABCC8-MODY). A Review of the Literature and Case Discussion. Curr Diab Rep. 2024 Sep;24(9):197–206.
4. Timmers M, Dirinck E, Lauwers P, Wuyts W, De Block C. ABCC8 variants in MODY12: Review of the literature and report of a case with severe complications. Diabetes Metab Res Rev. 2021 Nov;37(8):e3459.
5. Yalçıntepe S, Özgüç Çömlek F, Gürkan H, Demir S, Atlı Eİ, Atlı E, et al. The Application of Next Generation Sequencing Maturity Onset Diabetes of the Young Gene Panel in Turkish Patients from Trakya Region. J Clin Res Pediatr Endocrinol. 2021 Aug 23;13(3):320–31.
6. Çelebi HBG, Demiral M. Evaluation of variants in maturity onset of diabetes young related genes in Balıkesir region. Anatolian Curr Med J / ACMJ / acmj. 2023 Oct 27;5(4):421–5.
7. Lin L, Quan H, Chen K, Chen D, Lin D, Fang T. ABCC8-Related Maturity-Onset Diabetes of the Young (MODY12): A Report of a Chinese Family. Front Endocrinol (Lausanne). 2020;11:645.
8. Tang C, Meng L, Zhang P, Liang X, Dang C, Liang H, et al. Case Report: A Novel ABCC8 Variant in a Chinese Pedigree of Maturity-Onset Diabetes of the Young. Front Endocrinol (Lausanne). 2021;12:758723.
9. Bano G, Karunakaran V, Wei C. Monogenic Diabetes due to ABCC8/KCNJ11 Mutation: Case Study and Review of Literature. J Endo Meta Res. 2020 Apr 2;1(6):1–16.
10. Zamanfar D, Hashemi-Soteh SM, Ghazaiean M, Amoli M. Report of a Novel Mutation of ABCC8 Gene Related to MODY12 Phenotype. EC Gynaecology. 2022;11(11):25–30.
11. Antal Z. Maturity-Onset Diabetes of the Young (MODY): Genetic Causes, Clinical Characteristics, Considerations for Testing, and Treatment Options. Endocrines. 2021 Dec;2(4):485–501.
12. Nkonge KM, Nkonge DK, Nkonge TN. The epidemiology, molecular pathogenesis, diagnosis, and treatment of maturity-onset diabetes of the young (MODY). Clin Diabetes Endocrinol. 2020 Nov 4;6(1):20.
13. Jang KM. Maturity-onset diabetes of the young: update and perspectives on diagnosis and treatment. Yeungnam Univ J Med. 2020 Jan 9;37(1):13–21.
14. Broome DT, Pantalone KM, Kashyap SR, Philipson LH. Approach to the Patient with MODY-Monogenic Diabetes. J Clin Endocrinol Metab. 2021 Jan 1;106(1):237–50.
15. Peixoto-Barbosa R, Reis AF, Giuffrida FMA. Update on clinical screening of maturity-onset diabetes of the young (MODY). Diabetol Metab Syndr. 2020;12:50.
16. Colclough K, Patel K. How do I diagnose Maturity Onset Diabetes of the Young in my patients? Clin Endocrinol (Oxf). 2022 Oct;97(4):436–47.
17. Tshivhase A, Matsha T, Raghubeer S. Diagnosis and Treatment of MODY: An Updated Mini Review. Applied Sciences. 2021 Jan;11(20):9436.

https://doi.org/10.56303/jhnresearch.v4i1.347

18.Alwithenani R, Alzahrani J, Allugmani E, Hakami F. Co-inheritance of Rare Variants of Maturity-Onset Diabetes of the Young (MODY): A Case Report and Review of the Literature. Cureus. 2024 Sep;16(9):e69039.
19.Rafique I, Mir A, Saqib MAN, Naeem M, Marchand L, Polychronakos C. Causal variants in Maturity Onset Diabetes of the Young (MODY) – A systematic review. BMC Endocrine Disorders. 2021 Nov 11;21(1):223.
20.Ivanoshchuk DE, Shakhtshneider EV, Rymar OD, Ovsyannikova AK, Mikhailova SV, Fishman VS, et al. The Mutation Spectrum of Maturity Onset Diabetes of the Young (MODY)-Associated Genes among Western Siberia Patients. J Pers Med. 2021 Jan 18;11(1):57.

https://doi.org/10.56303/jhnresearch.v4i1.347