*American Journal of Medical Genetics Part A*

WILEY

AMERICAN JOURNAL OF medical genetics PART A

CASE REPORT

# Genotype and Clinical Phenotype of Monocarboxylate Transporter 1 Deficiency in Three Palestinian Children: Report of Two Novel Variants in the *SLC16A1* Gene

Imad Dweikat[1] | Moien Kanaan[2] | Hanin Kassem[2] | Huthaifa H. Ahmad[3]

[1]Metabolic Department, Faculty of Medicine, Arab American University, Jenin, Palestine | [2]Molecular Genetics Lab, Bethlehem University, Bethlehem, Palestine | [3]Arab American University, Jenin, Palestine

**Correspondence:** Imad Dweikat (imad.dweikat@aaup.edu)

**Received:** 29 December 2024 | **Revised:** 12 May 2025 | **Accepted:** 21 May 2025

**Funding:** The authors received no specific funding for this work.

**Keywords:** dehydration | ketoacidosis episodes | ketogenic stress | metabolic decompensation | trigger

## ABSTRACT

Monocarboxylate transporter 1 (MCT1) deficiency (OMIM# 616095), caused by variants in the *SLC16A1* gene (OMIM# 600682), is responsible for the transport of monocarboxylates across the plasma membrane. This condition is recognized as a rare genetic cause of impaired ketone body utilization in extrahepatic tissues, resulting in recurrent ketoacidosis triggered by fasting and infection. To date, only 17 patients with this disorder have been identified. Individuals with homozygous variants typically present at a younger age, exhibit developmental delays, and experience more severe ketoacidosis. We describe the genotype and clinical phenotype of three Palestinian children with MCT1 deficiency from two unrelated families. In an extended consanguineous family (Family A), whole exome sequencing identified a novel homozygous missense variant, *SLC16A1*_p.Gly25Val, in patient 1. Patient 2 was homozygous for the same variant. In unrelated family B, exome sequencing of patient 3 revealed another novel homozygous missense variant, *SLC16A1*_p.Leu403Phe. The clinical phenotypes and biochemical abnormalities were similar across all three patients, characterized by acute recurrent vomiting, severe dehydration, metabolic acidosis, and hyperuricemia. MCT1 deficiency should be considered in infants and children who experience recurrent ketoacidosis. We report two novel homozygous variants in the *SLC16A1* gene, further expanding the genotype–phenotype spectrum of this rare disorder.

## 1 | Introduction

3-Hydroxybutyrate, acetoacetate, and acetone are called ketone bodies. They are important alternative energy sources for maintaining blood glucose levels during fasting. Ketone bodies, however, are acids and cause ketoacidosis when accumulated. Succinyl-CoA:3-ketoacid CoA transferase (SCOT) deficiency and mitochondrial acetoacetyl-CoA thiolase (beta-ketothiolase or T2; ACAT1) deficiency are rare inherited metabolic disorders of ketone body utilization (Hori et al. 2015). Both SCOT and ACAT1 are involved in ketolysis, the breakdown of ketone bodies into the key cellular energy source, acetyl CoA.

Monocarboxylate transporter 1 (MCT1) is one of the transmembrane transporters encoded by the *SLC16* gene family. Among these, MCT1, MCT2, MCT3, and MCT4 transport monocarboxylates such as lactate, pyruvate, and ketone bodies. Monocarboxylate transporter 1 (SLC16A1, also called MCT1) has been reported as a rare disorder of ketone body utilization (Hori et al. 2015; Van Hasselt et al. 2014). Ketoacidosis, a

pathologic state, occurs when ketone formation exceeds ketone utilization. Typically, patients develop ketoacidosis during ketogenic stress such as starvation, febrile conditions, and physical stresses because ketone bodies produced in the liver accumulate due to defective utilization in extrahepatic tissues. Similar to diabetic ketoacidosis, the clinical consequences are characterized by vomiting, dehydration, and Kussmaul breathing that may progress to decreased consciousness and, ultimately, death. In contrast to diabetic ketoacidosis, patients with disorders of ketone body utilization characteristically have normal or low blood glucose levels (Van Hasselt et al. 2014).

MCT1 is responsible for transporting monocarboxylates including lactate, pyruvate, and ketone bodies across the plasma membrane (Van Hasselt et al. 2014; Stanescu et al. 2022). Dominant gain-of-function variants in the promoter region of the *SLC16A1* gene, causing abnormal expression of MCT1 in pancreatic β-cells, have been identified in patients with exercise-induced hyperinsulinemic hypoglycemia. Inactivating recessive homozygous or heterozygous variants in the *SLC16A1* gene have been identified in patients with ketone body utilization disorder (Stanescu et al. 2022).

The clinical phenotype of MCT1 deficiency is characterized by vomiting, severe ketoacidosis, and hypoglycemia and has been reported in patients with homozygous and heterozygous variants (Bozacı and Ünal 2022; Al-Khawaga et al. 2019). Patients with homozygous variants usually present at a younger age, have developmental delay, and more severe ketoacidosis. The age of presentation of patients with heterozygous variants varies from the neonatal period until childhood (Al-Khawaga et al. 2019; Balasubramaniam et al. 2015). A rare presentation was reported in a girl with frequent absence seizures for 3 years unresponsive to anticonvulsant therapy. Within 2 days after initiation of a ketogenic diet (KD), the seizure frequency dramatically reduced, but she developed metabolic acidosis and hypoglycemia, which resolved after discontinuing KD (Le et al. 2020).

There is increased evidence that metabolic stress is a major contributor to neurodegeneration through oxygen and glucose deprivation and that MCT1 plays a role in the responses of oligodendrocytes and oligodendrocyte precursor cells to metabolic and ischemic stresses, suggesting that MCT1 function could play an important role in the survival of oligodendrocytes and oligodendrocyte precursor cells in their response to ischemic white matter injury (Zhou et al. 2018).

Neuroimaging findings in MCT1 deficiency usually have a distinctive pattern of bilateral symmetrical bandlike T2 hyperintense signal abnormality at the gray-white matter interface involving the subcortical U fibers, most pronounced in the frontal lobes and insulae, as well as bilateral symmetrical T2 hyperintense signal abnormality in the basal ganglia and thalami (Al-Khawaga et al. 2019).

In this report, we present the clinical phenotype and molecular genetic analysis of three patients with MCT1 deficiency. To our knowledge, this is the first report of MCT1 deficiency in Palestine, with only 17 patients documented in the literature to date. We identified two novel homozygous missense variants in the *SLC16A1* gene, which further expands the genetic spectrum of this rare disorder.

## 2 | Patients and Methods

### 2.1 | Patients

Informed consent for detailed clinical and biochemical phenotyping and the publication of results was obtained from the patients' legal guardians. Ethical approval was provided by the Arab American University IRB committee (approval numbers 2022/C/10/N and 2024/A/3/C). This study adheres to the guidelines of the Declaration of Helsinki and local ethical committee protocols. This study describes the clinical manifestations, genetic analysis, and biochemical abnormalities of three Palestinian children with MCT1 deficiency. The diagnosis was based on the clinical phenotype, urine organic acid analysis, and whole exome sequencing. Clinical examination was performed for the 3 patients at the time of the diagnosis and during follow-up at the metabolic clinic.

### 2.2 | Sample Collection

Blood samples were collected from all three patients and DNA extraction was performed using a Qiagen Flexigene Kit (Qiagen, Hilden, Germany) according to the manufacturer's instructions. The concentration and purity of the extracted DNA were confirmed using a Nanodrop spectrophotometer (Thermo Fisher Scientific, Waltham, MA, USA). Informed consent for molecular genetic analysis was obtained from all participants.

### 2.3 | Molecular Analysis

Whole exome sequencing (WES) was performed on DNA samples from Patient 1 and Patient 3. Library preparation was carried out using the TruSeq Capture Exome Kit (Illumina). The probe set was designed to enrich 214,405 exons. After sequencing on NextSeq 500, data was aligned to the reference human genome (hg19) using a BWA aligner and variant calling by GATK (Genome Analysis Toolkit). The final list of variants was annotated by ANNOVAR using several databases of minor allele frequency such as Pop Freq Max as well as variant effect predictors such as SIFT, PolyPhen-2, and REVEL. Variants with low coverage, synonymous, predicted benign (SIFT, PolyPhen-2, REVEL), MAF > 1% on gnomAD, PopFreqMax, and our Palestinian in-house database were filtered out.

### 2.4 | Sanger Sequencing

Touchdown PCR was conducted in a 25 μL reaction mixture containing 50 ng of genomic DNA, 12.5 μL of HS Taq mix (PCRbio), 1 μL of forward primer (10 μM) 5′ GACACTCTGGCTGCTTCATG 3′, and 1 μL of reverse primer (10 μM) 5′ TGGATTTGACCTGCATTTTGGA 3′, with nuclease-free water added to reach the final volume. The cycling conditions included an initial denaturation at 95°C for 2 min, followed by 3 cycles of denaturation at 95°C for 30 s,

annealing at 63°C–55°C (descending by 3°C) for 30 s, and extension at 72°C for 30 s, concluding with a final extension at 72°C for 10 min. Sequencing reactions were performed using the BigDye Terminator v3.1 Cycle Sequencing Kit (Applied Biosystems) according to the manufacturer's protocol. Sequencing was carried out on an Applied Biosystems 3500 DNA Analyzer.

## 3 | Results

### 3.1 | Clinical Reports

We report three patients (two females and one male) with MCT1 deficiency. Patients 1 and 2 are from family A, while patient 3 is from an unrelated family B. All patients are offspring of consanguineous marriages and are alive at the time of the study. Symptoms in all three patients began before the age of 1 year.

Patient 1, an 8-year-old female from Family A, initially presented at 1 year of age with fever, recurrent vomiting, lethargy, and severe dehydration on physical examination. Laboratory findings at presentation included metabolic acidosis (pH 7.29, $HCO_3$ 8.3, $pCO_2$ 18), a serum lactic acid level of 2.3 mmol/L (reference: 0.5–2.5 mmol/L), serum ammonia at 77 μmol/L (reference: 35–80 μmol/L), and markedly elevated serum uric acid at 18 mg/dL (reference: 2.4–5.7 mg/dL). Qualitative urine organic acid analysis revealed significant excretion of lactic acid, 3-hydroxybutyric acid, and acetoacetic acid, while quantitative plasma amino acid analysis was unremarkable, and liver transaminases were normal. WES at 2½ years of age confirmed the diagnosis, identifying a novel homozygous missense variant (*SLC16A1*_p.Gly25Val). By age 8, the patient had experienced six episodes of ketoacidosis, the latest occurring at 6 years and 8 months. At her most recent follow-up, she demonstrated normal cognitive function, an unremarkable neurological exam, and excellent academic performance (Table 1).

Patient 2, a 7-year-old female from Family A, first presented at 4 months of age with recurrent vomiting, poor feeding, lethargy, and severe dehydration on physical examination. Initial laboratory findings indicated severe metabolic acidosis (pH 6.98, $HCO_3$ 3.8, $PCO_2$ 18), elevated serum lactic acid (2.4 mmol/L), normal serum ammonia (76 μmol/L), and markedly high uric acid (22 mg/dL). Qualitative urine organic acid analysis and quantitative plasma amino acid testing were not performed. A definitive diagnosis was established at 5 years of age based on clinical phenotype and *SLC16A1* gene sequencing, which revealed the same homozygous missense variant (*SLC16A1*_p.Gly25Val) previously identified in Patient 1 through WES.

Throughout her clinical course, she experienced five episodes of ketoacidosis, the most recent occurring at age 5. At her latest follow-up (7 years old), she exhibited normal cognitive function and an unremarkable neurological exam. However, she displayed hyperactivity and poor school performance. Although a formal diagnosis of attention deficit hyperactivity disorder (ADHD) was not pursued, the family declined referral to a pediatric neurologist for further evaluation (Table 1).

Patient 3, from unrelated family B, is a 1-year-and-8-month-old male who first presented at 6 months of age with fever, recurrent vomiting, lethargy, and respiratory distress. Physical examination revealed severe dehydration. Initial laboratory findings included metabolic acidosis (pH 7.14, $HCO_3$ 6, $pCO_2$ 10), with a serum lactic acid level of 1 mmol/L, ammonia of 72 μmol/L, and uric acid of 15.8 mg/dL. Similar to Patient 1, qualitative urine organic acid analysis demonstrated marked excretion of lactic acid, 3-hydroxybutyric acid, and acetoacetic acid. Quantitative plasma amino acid analysis and liver transaminases were within normal limits, and a brain MRI conducted during the first episode showed no abnormalities. WES identified a novel homozygous missense variant (*SLC16A1*_p.Leu403Phe).

Throughout his clinical course, the patient experienced four episodes of ketoacidosis, the most recent occurring at 1 year and 7 months of age. At his latest follow-up (1 year and 10 months), he exhibited normal cognitive function, an unremarkable neurological exam, and age-appropriate behavior and social interactions (Table 1).

The exome sequencing conducted on patients 1 and 3 identified both mitochondrial and copy number variants. No other clinically relevant findings associated with monocarboxylate transporters related to lactic acidosis or ketoacidosis were observed. The two identified variants were confirmed through Sanger sequencing and were found to segregate within the two studied families. Notably, the parents and all other family members who carried the two variants in a heterozygous state did not experience any episodes of ketoacidosis (see Figure 1).

## 4 | Discussion

In this study, we report the clinical and molecular genetic findings of three patients with MCT1 deficiency from two unrelated families, representing the first documented cases in Palestine. We identified two novel homozygous missense variants in the *SLC16A1* gene (p.Gly25Val and p.Leu403Phe), expanding the genetic spectrum of this rare disorder. Our patients presented with recurrent episodes of vomiting and severe ketoacidosis, consistent with the known phenotype of MCT1 deficiency. However, the absence of hyperammonemia, lactic acidosis, or liver dysfunction, along with distinctive neuroimaging findings, further refines the clinical characterization of this condition. These findings underscore the importance of considering MCT1 deficiency in the differential diagnosis of recurrent ketoacidosis, particularly in populations where consanguinity is common.

The p.Gly25Val and p.Leu403Phe variants identified in our patients are novel and were predicted to be pathogenic by in silico tools, including CADD and AlphaMissense (Cheng et al. 2023; Schubach et al. 2024). Both variants were absent from population databases and our in-house control cohort, supporting their likely deleterious impact on MCT1 function. These findings add to the growing list of pathogenic variants in the *SLC16A1* gene and highlight the genetic heterogeneity of MCT1 deficiency. Clinically, our patients exhibited the hallmark features of MCT1 deficiency, including recurrent ketoacidosis triggered by fasting or infection. However, the absence of hyperammonemia and lactic acidosis distinguishes this condition from other metabolic

**TABLE 1** | Clinical manifestations, laboratory findings, and genetic variants of the patients enrolled in the study.

**Clinical findings**

| Patient | Sex/Age/ Family | Age at onset of symptoms | Age at diagnosis | Trigger | Clinical manifestations | Number of episodes | Last episode | Neurological outcome |
|---|---|---|---|---|---|---|---|---|
| 1 | Female 8 years Family A | 1 year | 2½ years | Fever | Recurrent vomiting, severe dehydration, lethargy, metabolic acidosis, hypoglycemia, and hyperuricemia; 18 mg/dL (RR 2.4–5.7 mg/dL) | 6 | 6 years and 8 months | Normal cognition, behavior, and social interaction, excellent school performance. |
| 2 | Female 7 years Family A | 4 months | 5 years | No Trigger | Recurrent vomiting, poor feeding, lethargy, severe dehydration, metabolic acidosis, hyperuricemia; 22 mg/dL (RR 2.4–5.7) | 5 | 5 years | Normal cognition and speech. Has hyperactivity and suboptimal school performance. A formal diagnosis of ADHD was not made |
| 3 | Male 1 year 10 months Family B | 6 months | 11 months | Fever | Recurrent vomiting, lethargy, tachypnea, severe metabolic acidosis, hyperuricemia; 15.8 mg/dL, high CPK; 663 U/L | 4 | 1 year and 7 months | Normal cognition, speech, social interaction, behavior, and motor milestones |

**Laboratory findings**

| Initial blood gas pH/$PCO_2$/$HCO_3$ | Initial serum lactic acid mmol/L (normal 0.5–2.5 mmol/L) | Initial serum ammonia μmol/L (normal 35–80 μmol/L) | Qualitative urine organic acid analysis | Plasma amino acid analysis |
|---|---|---|---|---|
| 7.29/18/8.3 | 2.3 | 77 | Massive excretion of lactic acid and ketones (3-Hydroxybutyric and Acetoacetic acids) | Normal |
| 6.95/18/3.8 | 2.4 | 76 | Not performed | Not performed |
| 7.14/10/6 | 1 | 72 | Massive excretion of lactic acid and ketones (3-Hydroxybutyric and acetoacetic acids). | Normal |

**Genetic variants**

| Gene | Variant | Zygosity | In Silico prediction tools | Variant classification/ ACMG guidelines | CADD score | Alpha missense score |
|---|---|---|---|---|---|---|
| *SLC16A1* | NM_003051.4 c.74G>T (p.Gly25Val) | Homozygous | SIFT: Deleterious, PolyPhen: Probably Damaging | Novel/Variant of unknown significance (VUS) (PP1[a], PM2[b], PP3[c]) | 28 | 0.9562 |
| *SLC16A1* | NM_003051.4 c.74G>T (p.Gly25Val) | Homozygous | SIFT: Deleterious, PolyPhen: Probably Damaging | Novel/Variant of unknown significance (VUS) (PP1[a], PM2[b], PP3[c]) | 28 | 0.9562 |
| *SLC16A1* | NM_003051.4 c.1207C>T (p.Leu403Phe) | Homozygous | SIFT: Deleterious, PolyPhen: Possibly Damaging | Novel/Variant of unknown significance (VUS) (PM2[b], PP3[c]) | 27 | 0.9914 |

[a]PP1, or Pathogenic Supporting 1, is an ACMG/AMP criterion indicating co-segregation with disease.
[b]PM2, or Pathogenic Moderate 2, is an ACMG/AMP criterion that signifies a genetic variant's absence from controls (or at extremely low frequency if recessive) in Exome Sequencing Project, 1000 Genomes Project, GnomAD, or Exome Aggregation Consortium.
[c]PP3, pathogenic supporting: For a missense or a splicing region variant, computational prediction tools unanimously support a deleterious effect on the gene.

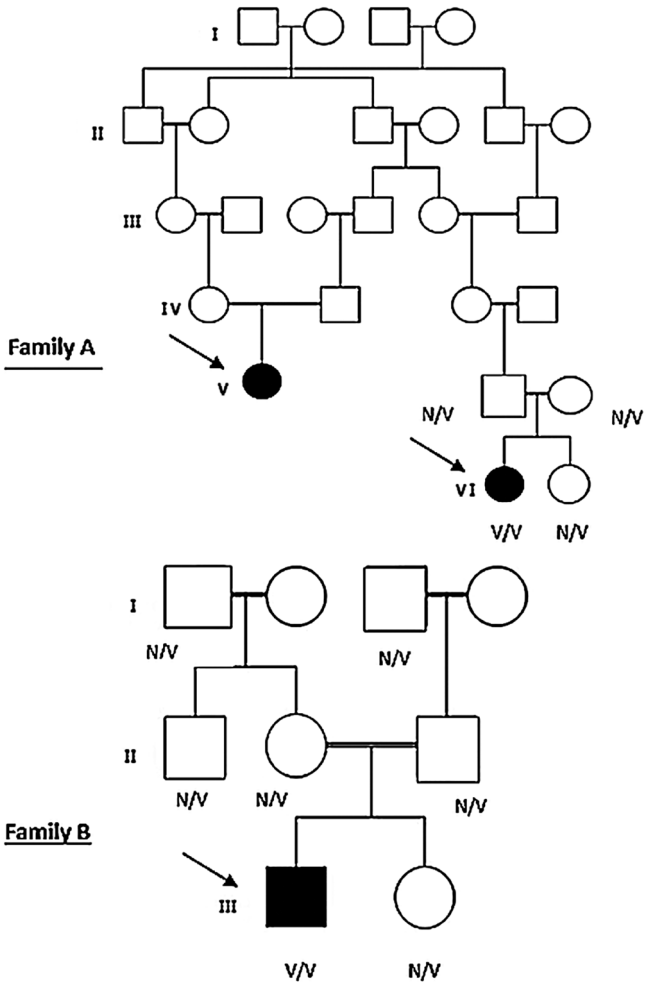


**FIGURE 1** | Pedigrees of the two families (A and B) with MCT1 deficiency. Probands are marked with a black arrow (V/V). Heterozygous (carrier) individuals are indicated as (N/V).

disorders, such as organic acidemias or mitochondrial diseases. Additionally, the presence of hyperuricemia in all three patients, likely secondary to ketoacidosis and hypovolemia, may provide a new biochemical clue that may aid in diagnosis.

Our findings align with previous reports of MCT1 deficiency, which describe recurrent ketoacidosis, normal or low blood glucose levels, and normal serum ammonia and lactate levels (Van Hasselt et al. 2014; Stanescu et al. 2022). However, the neuroimaging findings in our patients add to the limited data on central nervous system involvement in this disorder. While brain MRI in one patient was normal, others have reported bilateral symmetrical T2/FLAIR hyperintense lesions in the subcortical white matter, basal ganglia, and thalami (Al-Khawaga et al. 2019; Nicolas-Jilwan et al. 2020). These findings suggest that MCT1 deficiency may affect brain regions with high energy demands, particularly during metabolic stress. The role of MCT1 in maintaining brain energy homeostasis is further supported by its upregulation during fasting, which ensures a sustained supply of ketone bodies to the brain (Chasseigneaux et al. 2024).

The phenotypic variability observed in MCT1 deficiency, ranging from severe early-onset disease in homozygous patients to milder or later-onset presentations in heterozygous variants, underscores the complex interplay between genetic and environmental factors. For example, patients with heterozygous variants may remain asymptomatic or present with symptoms, such as recurrent vomiting or hypotonia, during infancy (Bozacı and Ünal 2022; Balasubramaniam et al. 2015). A rare case of a heterozygous carrier presenting with absence seizures responsive to a ketogenic diet further highlights the diverse clinical manifestations of this disorder (Le et al. 2020). These observations suggest that additional genetic or environmental modifiers may influence the severity and presentation of MCT1 deficiency.

While our study provides valuable insights into the genetic and clinical spectrum of MCT1 deficiency, it has several limitations. First, the small sample size limits the generalizability of our findings. Second, functional studies to confirm the pathogenicity of the identified variants were not performed, although in silico predictions strongly support their deleterious effects. Third, long-term follow-up data on neurodevelopmental outcomes and the impact of recurrent metabolic crises on brain function are lacking. Future studies should address these limitations by including larger cohorts, conducting functional assays, and evaluating long-term outcomes.

## 5 | Conclusions

MCT1 deficiency should be considered in infants and children who present with recurrent episodes of ketoacidosis. We report two novel missense variants in the *SLC16A1* gene, which further expand the genetic spectrum of MCT1 deficiency. As observed in other patients with homozygous variants, the clinical phenotype was characterized by infantile-onset recurrent ketoacidosis episodes, which decreased in frequency with advancing age.

### Author Contributions

**Imad Dweikat:** writing – review and editing, writing – original draft, software, formal analysis, conceptualization. **Moien Kanaan:** writing – review and editing, formal analysis, data curation. **Hanin Kassem:** writing – review and editing, data curation. **Huthaifa H. Ahmad:** software, formal analysis.

### Acknowledgments

The authors acknowledge the staff in the molecular genetic lab at Istishari Arab Hospital for participating in the molecular genetic analysis of the three patients.

### Ethics Statement

Ethical approval was provided by the Arab American University IRB committee (approval numbers 2022/C/10/N and 2024/A/3/C). This study adheres to the guidelines of the Declaration of Helsinki and local ethical committee protocols.

### Consent

Informed consent for publication was obtained from all the patients' guardians.

### Conflicts of Interest

The authors declare no conflicts of interest.

## Data Availability Statement

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

## References


Al-Khawaga, S., J. AlRayahi, F. Khan, et al. 2019. "A SLC16A1 Mutation in an Infant With Ketoacidosis and Neuroimaging Assessment: Expanding the Clinical Spectrum of MCT1 Deficiency." *Frontiers in Pediatrics* 7: 299. https://doi.org/10.3389/fped.2019.00299.

Balasubramaniam, S., B. Lewis, L. Greed, et al. 2015. "Heterozygous Monocarboxylate Transporter 1 (MCT1, SLC16A1) Deficiency as a Cause of Recurrent Ketoacidosis." In *JIMD Reports*, edited by E. Morava, M. Baumgartner, M. Patterson, S. Rahman, J. Zschocke, and V. Peters, vol. 29, 33–38. Springer. https://doi.org/10.1007/8904_2015_519.

Bozacı, A. E., and A. T. Ünal. 2022. "Rare Cause of Ketolysis: Monocarboxylate Transporter 1 Deficiency." *Turkish Journal of Pediatrics* 64, no. 4: 741–746. https://doi.org/10.24953/turkjped.2021.4915.

Chasseigneaux, S., V. Cochois-Guégan, L. Lecorgne, et al. 2024. "Fasting Upregulates the Monocarboxylate Transporter MCT1 at the Rat Blood-Brain Barrier Through PPAR δ Activation." *Fluids and Barriers of the CNS* 21, no. 1: 33. https://doi.org/10.1186/s12987-024-00526-8.

Cheng, J., G. Novati, J. Pan, et al. 2023. "Accurate Proteome-Wide Missense Variant Effect Prediction With AlphaMissense." *Science* 381, no. 6664: eadg7492. https://doi.org/10.1126/science.adg7492.

Hori, T., S. Yamaguchi, H. Shinkaku, et al. 2015. "Inborn Errors of Ketone Body Utilization." *Pediatrics International* 57, no. 1: 41–48. https://doi.org/10.1111/ped.12585.

Le, A., M. Yeganeh, D. Buhas, M.-J. Trempe, and K. A. Myers. 2020. "Monocarboxylate Transporter-1 Deficiency Results in Severe Metabolic Acidosis With Ketogenic Diet in Early Onset Absence Epilepsy: Case Report." *Seizure* 74: 31–32. https://doi.org/10.1016/j.seizure.2019.11.008.

Nicolas-Jilwan, M., R. Medlej, R. A. Sulaiman, and M. AlSayed. 2020. "The Neuroimaging Findings of Monocarboxylate Transporter 1 Deficiency." *Neuroradiology* 62, no. 7: 891–894. https://doi.org/10.1007/s00234-020-02435-7.

Schubach, M., T. Maass, L. Nazaretyan, S. Röner, and M. Kircher. 2024. "CADD v1.7: Using Protein Language Models, Regulatory CNNs and Other Nucleotide-Level Scores to Improve Genome-Wide Variant Predictions." *Nucleic Acids Research* 52, no. D1: D1143–D1154. https://doi.org/10.1093/nar/gkad989.

Stanescu, S., I. Bravo-Alonso, A. Belanger-Quintana, et al. 2022. "Mitochondrial Bioenergetic is Impaired in Monocarboxylate Transporter 1 Deficiency: A New Clinical Case and Review of the Literature." *Orphanet Journal of Rare Diseases* 17, no. 1: 243. https://doi.org/10.1186/s13023-022-02389-4.

Van Hasselt, P. M., S. Ferdinandusse, G. R. Monroe, et al. 2014. "Monocarboxylate Transporter 1 Deficiency and Ketone Utilization." *New England Journal of Medicine* 371, no. 20: 1900–1907. https://doi.org/10.1056/NEJMoa1407778.

Zhou, P., T. Guan, Z. Jiang, M. Namaka, Q. Huang, and J. Kong. 2018. "Monocarboxylate Transporter 1 and the Vulnerability of Oligodendrocyte Lineage Cells to Metabolic Stresses." *CNS Neuroscience & Therapeutics* 24, no. 2: 126–134. https://doi.org/10.1111/cns.12782.