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Case Report

Nutrition Section

Ketogenic Diet for Seizure Management in Glucose Transporter Type 1 Deficiency Syndrome: A Case Report

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ABSTRACT

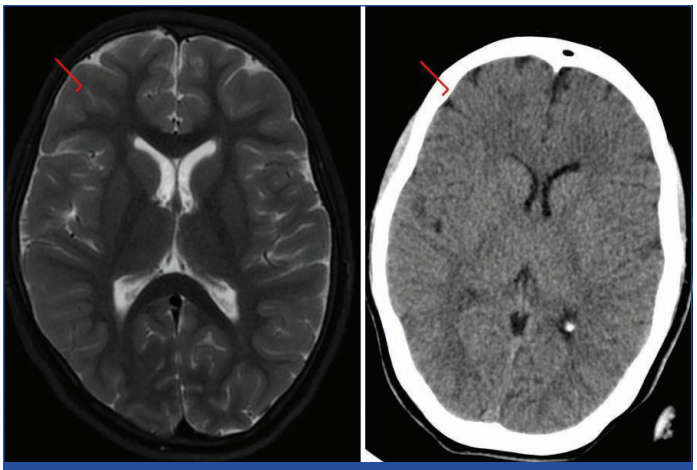
Glucose transporter Type 1 (GLUT1) deficiency syndrome is a rare genetic disorder impairing glucose transport across the blood-brain barrier, leading to reduced brain glucose availability and neurological symptoms, including epilepsy. The Ketogenic Diet (KD), high in fat and low in carbohydrates, induces ketosis, providing ketone bodies as an alternative brain fuel bypassing GLUT1 transport. This compensates for glucose deficiency, stabilising neuronal activity and reducing seizure frequency in GLUT1 deficiency. This case is of a 10-year-old girl with GLUT1 deficiency syndrome, developmental delay, SLC2A1 gene mutation and refractory epilepsy with 2-3 weekly seizures despite multiple Antiseizure Medications (ASMs). A South Indian-style KD, using traditional household ingredients, was initiated as medical nutrition therapy. Remarkable improvements were observed, a 50% reduction in seizures within one month, 80% reduction by three months and complete seizure freedom by the fourth month. Developmental progress accompanied seizure control and the diet was well-tolerated, maintaining stable nutritional status. This case highlights the efficacy of a culturally tailored KD in managing GLUT1 deficiency, emphasising its potential as a form of therapeutic treatment. Ongoing parental support and supervision were critical for ensuring dietary adherence and optimising outcomes.

Keywords: Epilepsy, Neurodevelopmental delay, SLC2A1 gene mutation

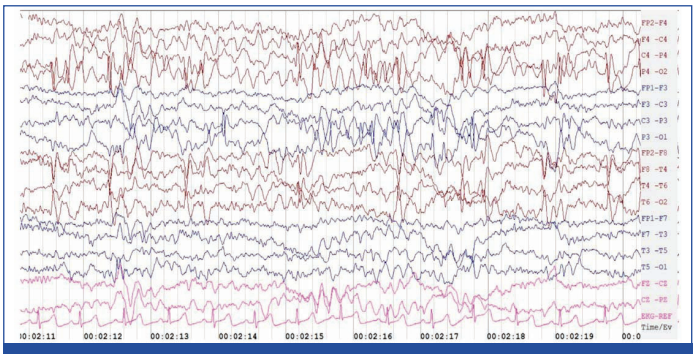
CASE REPORT

A 10-year-old girl from Southern part of India was a known case of GLUT1 Deficiency Syndrome since two years of age presented with complaints of developmental delay as assessed by paediatric epileptologist and seizure disorder, with two to three episodes per week. The patient has been on a regimen of three ASMs such as Sodium Valproate 60 mg/kg/day Levetiracetam 50 mg/kg/day and Clobazam 1 mg/kg/day for six years. She comes from a joint family with no reported history of seizures. The patient was noted to have developmental delays. Antenatal scans were normal, and there was no history of Neonatal Intensive Care Unit (NICU) admission postbirth. She was a term baby, delivered via Normal Vaginal Delivery with a birth weight of 2.8 kg, and immunisations were up-to-date according to the National Immunisation Schedule (NIS). The patient was the first child of a consanguineous marriage. She was exclusively breastfed for one year and then transitioned to appropriate complementary feeding. Currently, the child has been following the regular family meals mixed diet. Subjective data indicated normal gastrointestinal function and refreshing sleep patterns. On clinical examination, there was no overt signs and symptoms of nutritional deficiencies noted. Biochemical analysis were within normal ranges. At baseline before starting KD the plasma blood glucose was 90 mg/dL and urine ketone was negative. Neuroimaging, tests like Magnetic Resonance Imaging (MRI) and Computed Tomography (CT) of the brain was performed and, were noted as normal [Table/Fig-1,2]. However, an Electroencephalogram (EEG) revealed developmental epileptic encephalopathy [Table/Fig-3].

Genetic evaluation identified a pathogenic variation in the SLC2A1 gene. No obvious signs or symptoms of nutritional deficiencies were detected during the clinical evaluation. A thorough dietary assessment confirmed that the child's diet was sufficient in both quality and quantity, with no reported food allergies. Nutritional risk assessment, conducted using the STRONGkids nutrition screening tool [1], indicated a medium risk of malnutrition. At baseline before starting KD the triceps skin fold thickness was 6 mm and the World Health Organisation (WHO) score was below 1.



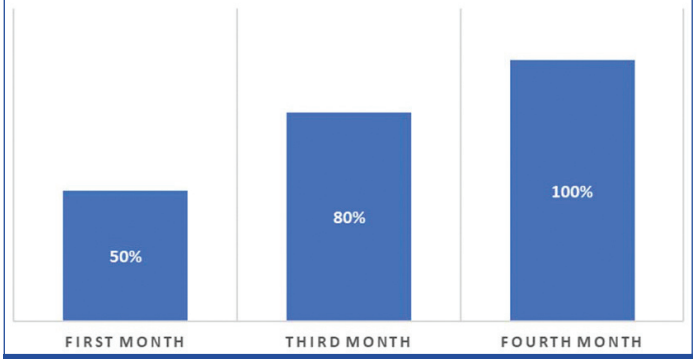
[Table/Fig-1]: Magnetic Resonance Imaging (MRI) T2 axial brain.
[Table/Fig-2]: Computed Tomography (CT) brain. (Images from left to right)



[Table/Fig-3]: Electroencephalogram (EEG)-developmental epileptic encephalopathy.

Therapeutic Nutritional Care was administered utilising the Nutrition Care Process Model [2]. The intervention began with initiating South Indian-style KD utilising traditional household ingredients following a Non-Fasting KD Protocol, comprising 5% carbohydrates, 31% protein, and 64% fat respectively. By the third day of starting the diet, the patient reached a urine ketone level of 4+. Following this, a 2:1 KD was introduced on the fourth day, comprising 9% carbohydrates,

9% protein, and 82% fat. Parents received thorough counseling on maintaining the KD at home. They were trained to monitor urine ketone levels and keep a seizure diary. Weekly monitoring was conducted through phone and video consultations, with necessary adjustments to caloric intake and diet ratios to ensure a 4+ urine ketone level throughout the day. Following the implementation of a home-based KD, there was a 50% reduction in seizure frequency within the first month. The patient remained on three ASMs while adhering to a 2:1 KD. By the third month, seizure frequency had decreased by 80%, and by the fourth month, the patient was completely seizure-free [Table/Fig-4]. The diet was well tolerated, and developmental improvements were observed. According to the parents, the child has become more cooperative, engaging in play and socialising with peers [Table/Fig-5]. The child's nutritional status has also improved, with an age-appropriate increase in height and weight [Table/Fig-6]. Currently in the eighth month of the KD with monthly follow-ups, the child remains seizure-free and continues to maintain 4+ urine ketone levels throughout the day. The diet is well tolerated, and ASMs are being continued at a reduced dose.



[Table/Fig-4]: Percentage reduction in seizure following ketogenic diet.

Aspect	Before ketogenic diet	After ketogenic diet
Cooperation	Not cooperative	More cooperative
Socialisation	Not socialising with others	Socialising with peers
Playfulness	Not playing	Actively playing

[Table/Fig-5]: Developmental assessment before and after nutrition intervention.

Parameter	Before	After
STRONGkids score	Medium risk	Low risk
Height (cm)	132	135
Weight (kg)	25	30
BMI (kg/m^2)	14.36	16.48
Arm circumference (cm)	30	32

[Table/Fig-6]: Nutrition assessment before and after nutrition intervention.

DISCUSSION

GLUT1 deficiency syndrome is estimated to occur in approximately 1 in 30,000 to 50,000 live births worldwide. This prevalence can differ based on geographical and demographic variations, but this range is widely accepted. Due to the rarity of this condition and the possibility of underdiagnosis, determining the exact incidence is challenging. However, it generally aligns with prevalence estimates, with new cases falling within the range of 1 in 30,000 to 50,000 births [3]. The KD is recognised as a highly effective treatment for paediatric patients with GLUT1 Deficiency Syndrome (GLUT1DS), a genetic disorder that impairs glucose transport across the blood-brain barrier. Long-term adherence to KD has demonstrated a favourable safety profile in terms of anthropometric measurements, body composition, resting energy expenditure and biochemical parameters. Additionally, there is no evidence suggesting significant adverse effects on the nutritional status of children and adolescents [4,5]. Early initiation of KD is crucial to maximise therapeutic benefits and transitioning to alternative dietary approaches can improve long-term adherence while managing potential side-effects [6-8]. A study conducted by Kass HR et al., in 2016 found that nearly all patients with GLUT1 deficiency syndrome who followed dietary therapies for extended periods achieved excellent seizure control, often without the need for anticonvulsant medications [9]. Early diagnosis and appropriate treatment are essential for individuals with GLUT1DS, emphasising the importance of maintaining a KD with an appropriate balance of ketogenic and non ketogenic elements to ensure sufficient energy intake. Personalised and structured nutritional management plays a critical role in supporting growth, development and overall wellbeing [10].

In this case, a 10-year-old female diagnosed with GLUT1DS, born to consanguineous parents, presented with developmental delays and seizure disorders. Despite normal antenatal scans and no history of NICU admissions, she exhibited tremors, gait disturbances and speech delays. EEG results indicated developmental epileptic encephalopathy, while MRI and CT scans appeared normal. Genetic testing confirmed a pathogenic variant in the SLC2A1 gene. A home-based KD led to a 50% reduction in seizure frequency within one month, an 80% reduction within three months, and complete seizure cessation by the fourth month. The Non Fasting Ketogenic Diet Protocol was used to initiate KD, incorporating a carbohydrate washout diet that enabled the patient to achieve ketosis (4+ ketones) without fasting. This washout phase, lasting 3 to 7 days, differed from the standard fasting method. The prescribed diet was extremely low in carbohydrates (5 g), with normal protein intake and increased fat consumption. This approach depletes stored liver glycogen, facilitating a metabolic shift toward fat utilisation. The subsequent production of ketone bodies (acetoacetic acid, beta-hydroxybutyric acid, and acetone) provides an alternative energy source for the brain. As this method does not require fasting, hospitalisation is unnecessary, significantly reducing treatment costs. This innovative dietary strategy effectively managed the patient's condition. Fat metabolism plays a crucial role in seizure control by producing ketones, which serve as an alternative brain energy source. Ketones stabilise neuronal activity and enhance inhibitory neurotransmitters like GABA, reducing seizure frequency. The patient tolerated the diet well and exhibited notable developmental improvements. According to the parents, the child, who was previously uncooperative and socially withdrawn, became more engaged, cooperative and interactive with peers after following KD. A lipid profile assessment after four months of KD initiation revealed normal results. This case highlights the effectiveness of KD as an intervention for GLUT1DS and underscores the importance of parental support in ensuring dietary adherence for optimal patient outcomes. South Indian cuisine is predominantly carbohydrate-rich, with rice being a staple, followed by proteins and fats [11]. However, KD requires a high intake of fats, moderate protein and minimal carbohydrates [12]. Given the child's South Indian background, the KD was adapted to align with her cultural food preferences while maintaining protocol adherence. Instead of limiting food choices to a narrow range of high-fat options, the diet plan incorporated diverse food groups to meet nutritional needs while controlling seizures. The customised KD included traditional South Indian dishes such as idli, dosa, upma, vegetable rice, biryani, fruits, milkshakes, and non vegetarian options. Since KD is a long-term management approach for seizures, it was crucial to ensure that the diet was not only effective but also sustainable and acceptable for both the child and her family. By tailoring the diet to her eating habits and cultural background, adherence was improved while maintaining seizure control. The child was closely monitored for four months and remained seizure-free throughout this period. Following this, the parents received comprehensive training to continue KD regimen at home. The child is now in her eighth month on the diet, attending monthly follow-up sessions and remains seizure-free, consistently showing 4+ urine ketones throughout the day. She continues to tolerate the diet well and her ASMs dosage has been gradually reduced.

CONCLUSION

The success of KD, as demonstrated in this case study, highlights the critical role of early diagnosis, strict dietary adherence and continuous parental involvement. It is also important to emphasise that the KD can be effectively implemented using familiar and acceptable foods within the family setting, leading to a reduction in seizure frequency and notable improvements in developmental milestones without relying on commercial supplements. These significant outcomes underscore the value of early dietary intervention in managing drug-resistant epilepsy and the essential contribution of a medical nutrition therapist.

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