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Clinical Spectrum, Neuroimaging, Dietary Management, and Outcomes in Glutaric Aciduria Type I: A Case Series from a Tertiary Metabolic Centre in India

Garvita Kharbanda[1*], Sirimavo Nair[1] and Priyanshu Mathur[2]

[1]*Department of Foods and Nutrition, Faculty of Family and Community Sciences, The Maharaja Sayajirao University of Baroda, Vadodara, Gujarat, India.*

[2]*Nodal Centre for Rare Disease, JK Lone Hospital, SMS Medical College, Jaipur, India.*

[*]garvita.k-fnphd@msubaroda.ac.in (Corresponding Author)

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ABSTRACT

Background: Glutaric aciduria type I (GA1) is a rare autosomal recessive neurometabolic disorder caused by a deficiency of glutaryl-CoA dehydro-genase, leading to the accumulation of glutaric acid, 3-hydroxyglutaric acid, and glutarylcarnitine. The condition predominantly affects the basal ganglia and cerebral cortex and is associated with acute neuroregression, dystonia, and macrocephaly. Early diagnosis and dietary management significantly improve outcomes, but delays are common in low-resource settings.

Purpose: This study aimed to describe the clinical spectrum, diagnostic challenges, neuroimaging features, treatment strategies, and short-term out-comes of children with Glutaric Aciduria Type I (GA1) managed at a ter-tiary care metabolic center in Rajasthan, India, thereby highlighting the importance of early recognition and timely dietary intervention in improving prognosis.

Methods: We conducted a retrospective review of children diagnosed with GA1 at a tertiary care metabolic center in Rajasthan, India, between June 2023 to September 2024. Diagnosis was based on clinical features, bio-chemical analysis using tandem mass spectrometry (TMS) and gas chroma-tography-mass spectrometry (GC-MS), neuroimaging, and where available, genetic testing. Clinical presentation, neuroimaging findings, treatment, and outcomes were analyzed.

Results: Out of 44 children with suspected inborn errors of metabolism evaluated during the study period, 7 (18.4%) were diagnosed with GA1. The mean age at symptom onset was 7.4 ± 2.3 months, and mean age at diagnosis was 21.5 ± 16.7 months. Macrocephaly was present in 85.7%, and 71.4% had acute encephalopathic crises triggered by infections. All children exhibited dystonia; two also had spastic quadriparesis. Neuroimaging showed frontotemporal atrophy with open opercula in all cases and basal ganglia changes in six. Biochemical testing confirmed elevated glutarylcarnitine (C5DC) in all patients, and urine organic acid analysis revealed elevated glutaric and 3-hydroxyglutaric acid in six. Genetic testing in three children identified GCDH mutations, including c.1204C>T in two. A lysine-restricted diet, carnitine supplementation, and emergency care procedures were used to treat every child. Three children remained severely disabled, two had moderate dystonia, and three had minimal deficits after an average follow-up of 18.2 ± 6.3 months.

Conclusions: In infants with dystonia, developmental delay or regression and macrocephaly, GA1 must be suspected, particularly when combined with distinctive neuroimaging findings. Results can be greatly enhanced by early diagnosis and the start of dietary and supportive therapy. Expanded use of genetic counseling, early dietary intervention, and newborn screening is necessary to lower the long-term morbidity linked to GA1 in settings with limited resources.

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1. Introduction

An autosomal recessive neurometabolic disorder known as glutaric aciduria type I (GA1) is caused by a lack of glutaryl-CoA dehydrogenase, a mitochondrial enzyme involved in the oxidative breakdown of tryptophan, lysine, and hydroxylysine. In bodily tissues and fluids, the enzyme defect causes the accumulation of glutaric acid (GA), 3-hydroxyglutaric acid (3-OH-GA), and glutarylcarnitine (C5DC) (Chace *et al.*, 2013; Kölker *et al.*, 2003). The neurotoxicity of these metabolites mainly affects cortical neurons and the basal ganglia. As a result, most patients experience irreversible

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neuronal damage and macrocephaly if treatment is delayed after birth. Clinically, GA1 typically manifests between 6 and 18 months of age with acute encephalopathic crises, developmental delay, and macrocephaly, usually brought on by infections or vaccinations (Strauss *et al.*, 2003; Hedlund *et al.*, 2006). Bilateral striatal necrosis may develop in such situations, leading to progressive neurodevelopmental impairment, severe dystonia, and spasticity. All of these are feasible, but the worst results will occur if prompt action is not taken to stop further deterioration (Harting *et al.*, 2009; Boy *et al.*, 2017). Frontotemporal atrophy with open opercula, basal ganglia involvement, and white matter changes are all characteristics of MRI findings that are crucial for the early identification of this disease entity (Harting *et al.*, 2009; Neumaier-Probst *et al.*, 2004). It is also possible for subdural hematomas to be mistaken for non-accidental injuries in infants (Vester *et al.*, 2016). Increased levels of C5DC on tandem mass spectrometry (TMS), higher concentrations of glutaric and 3-hydroxyglutaric acids as measured by gas chromatography-mass spectrometry (GC-MS), and GCDH gene mutation analysis are used to confirm the diagnosis (Gupta *et al.*, 2018; Narayanan *et al.*, 2011).

Newborn screening has been significantly expanded to show considerable advantages in terms of making an early presymptomatic diagnosis and the institution of therapy (Lindner *et al.*, 2011). However, due to the lack of universal screening under resource-constrained countries like India, there is a lag in diagnosis that results in poor outcomes (Kamate *et al.*, 2012; Sarangi *et al.*, 2017). Management of GA1 involves a lifelong lysine- and tryptophan-restricted diet, L-carnitine supplementation to facilitate detoxification, and emergency protocols during catabolic stress (Boy *et al.*, 2017; Kölker *et al.*, 2006). Use of lysine-free, tryptophan-reduced medical foods is crucial to prevent accumulation of toxic metabolites, and timely dietary intervention can result in normal or near-normal neurodevelopment (Kölker *et al.*, 2011; Saudubray *et al.*, 2016). In India, most published data on GA1 are limited to case reports and small case series (Gupta *et al.*, 2018; Kamate *et al.*, 2012), and comprehensive regional data remain scarce. This study aims to bridge this gap by presenting the clinical profile, neuroimaging features, biochemical findings, and outcomes of children diagnosed with GA1 at a tertiary metabolic center in Western India. Unlike previous Indian reports limited to single cases or brief series, the present study provides one of the largest regional case series from Rajasthan with systematic dietary adherence and outcome evaluation over 18 months.

2. Methodology

An observational study was conducted at the Centre for Rare Disease in Jaipur, Rajasthan, India, and other tertiary care hospitals catering to the needs of children with inborn errors of metabolism (IEM). The study included children diagnosed with Glutaric Aciduria Type I (GA1) over a one-year period from June 2023 to September 2024. The objective was to analyze the clinical characteristics, biochemical and neuroimaging findings, treatment approaches, and follow-up outcomes of children diagnosed with GA1 at our tertiary metabolic center. All suspected IMD cases were initially screened using tandem mass spectrometry (TMS) for acylcarnitine profile and GC–MS for urinary organic acids. GA1 diagnosis was confirmed biochemically in all cases; genetic confirmation was available in three children, which were included if they presented with clinical features suggestive of a neurometabolic disorder, such as macrocephaly, developmental delay or regression, dystonia, or seizures, and had a confirmed biochemical diagnosis of GA1. Confirmation was based on elevated glutarylcarnitine (C5DC) levels on tandem mass spectrometry (TMS) performed on dried blood spots and/or increased glutaric acid and 3-hydroxyglutaric acid levels detected on urine gas chromatography-mass spectrometry (GC-MS) (Chace *et al.*, 2003; Kölker *et al.*, 2006). Additionally, all children underwent brain magnetic resonance imaging (MRI), and characteristic radiological findings such as frontotemporal atrophy with open opercula (bat wing appearance), basal ganglia changes, and periventricular white matter abnormalities were assessed in correlation with clinical features (Harting *et al.*, 2009; Neumaier-Probst *et al.*, 2004).

Clinical data were collected from patient records and included age at symptom onset, age at diagnosis, sex, history of consanguinity, presenting symptoms, neurological findings including movement disorders and seizures, and anthropometric parameters such as head circumference. Standardized neurodevelopmental screening instruments were used to record the developmental history at the time of diagnosis and during follow-up appointments. We took careful note of the occurrence and pattern of spasticity, dystonia, and milestone regression. The type of precipitating factors and the future trajectory were examined for children who suffered from acute metabolic crises (Boy *et al.*, 2017). Standardized developmental screening instruments such as the Developmental Screening Test (DST) by Bharat Raj J., in conjunction with structured clinician observation and caregiver interviews, were used to evaluate neurodevelopmental outcomes. Accredited metabolic laboratories used dried blood spot samples to obtain biochemical confirmation via TMS. Urine samples were analyzed for organic acids using GC-MS (Chace *et al.*, 2003). Sanger sequencing or next-generation sequencing of the GCDH gene was used for genetic testing when it was feasible, and parental samples were used when necessary to confirm mutations (Gupta *et al.*, 2018). Following

diagnosis, dietary intervention was given to all children, including a low-protein lysine-restricted diet augmented with medical nutrition therapy. Tandem mass spectrometry (TMS) shows elevated C5DC levels. Gas chromatography-mass spectrometry (GC-MS) shows elevated glutaric and 3-hydroxyglutaric acid concentrations, and GCDH gene mutation analysis confirms the diagnosis (Gupta *et al.*, 2018; Narayanan *et al.*, 2011).

L-carnitine supplementation was initiated at a dose of 100 mg/kg/day to facilitate detoxification (Boy *et al.*, 2017). Families were counseled regarding strict avoidance of natural protein-rich foods such as meat, dairy, eggs, legumes, and soy products. Emergency dietary protocols were shared with caregivers to be implemented during periods of fever, infection, or reduced oral intake, with the goal of preventing catabolic crises (Saudubray *et al.*, 2016). Inclusion criteria include children ≤10 years with clinical suspicion of GA1 and confirmed biochemical diagnosis. Children with secondary macrocephaly, leukodystrophies, or unconfirmed metabolic results were excluded from the study. Ethical approval for the study was obtained from the Institutional Ethics Committee of the Department Research Committee (IECHR/FCSc/Ph.D/2023/10; approval date – June 2023) and the affiliated Medical College (Approval No. 2023/14217; dated September 2023).

3. Results

A total of 44 children with suspected inborn errors of metabolism were evaluated at our center between June 2023 and September 2024. Of these, 7 children (18.4%) were diagnosed with Glutaric Aciduria Type I (GA1) based on a combination of clinical features, biochemical markers, and characteristic neuroimaging findings (Table-1). The cohort included four males and three females. The mean age at symptom onset was 7.4 ± 2.3 months, while the mean age at diagnosis was 21.5 ± 16.7 months. A positive history of consanguinity was reported in four families (57.1%). Developmental delay was the most consistent presenting complaint, observed in all seven children. Acute encephalopathic crises following febrile illnesses were reported in five children (71.4%) and were associated with regression of previously acquired milestones. Macrocephaly was present in six children (85.7%), either noted at birth or developing in infancy. All children exhibited movement disorders, with dystonia being the predominant feature. Two children also demonstrated spastic quadriparesis. Notably, two children with a more insidious onset, both diagnosed after 24 months of age, had chronic developmental delay and slowly progressive dystonia without documented acute decompensation episodes.

Table 1 summarizes the individual clinical and radiological characteristics of the seven children diagnosed with Glutaric Aciduria Type I (GA1). While the age at diagnosis varied greatly, with some cases experiencing delays of more than a year, the age at symptom onset ranged from 5 to 10 months. Five children were reported to have experienced acute metabolic crises, and six were found to have macrocephaly. Two of the children had seizures, and all but one had developmental delays. Across the cohort, movement disorders were noted, especially dystonia with or without spasticity. All patients had frontotemporal atrophy, and six had involvement of the basal ganglia according to neuroimaging. Three patients had periventricular or deep white matter abnormalities, and one patient had bilateral subdural hemorrhages. The follow-up period was between 12 and 24 months. For every patient, neuroimaging was available. All seven children had the classic findings of frontotemporal atrophy with open opercula or a bat's wing appearance. Six patients had basal ganglia involvement, mainly affecting the putamen and caudate. Two children with delayed diagnosis exhibited additional periventricular white matter changes and generalized cerebral atrophy. One child also had bilateral subdural collections, potentially related to cortical atrophy and bridging vein rupture.

Table 1: Clinical, Radiological, and Outcome Features of Children with Glutaric Aciduria Type I

Patient ID	Age of Onset & Sex	Age at Diagnosis (months)	Consanguinity	Macrocephaly	Developmental Delay	Acute Metabolic Crisis	Seizures	Movement Disorder	MRI Findings – Fronto-temporal Atrophy	Basal Ganglia Changes	Subdural Hemorrhage	White Matter Changes	Follow-up (months)
1	6 m, Male	12	+	+	+	+	–	Dystonia	+	+	–	–	24
2	8 m, Female	22	+	+	+	+	–	Dystonia (UL)	+	+	–	–	18
3	7 m, Female	30	–	+	+	+	+	Dystonia, Spasticity	+	+	+	+	20

4	6 m, Male	9	+	+	+	–	–	Dystonia (UL)	+	–	–	–	12
5	5 m, Male	6	–	–	+	–	–	Dystonia	+	–	–	–	16
6	9 m, Female	36	+	+	+	+	+	Dystonia, Spasticity	+	+	–	+	22
7	10 m, Male	24	+	+	+	+	–	Dystonia	+	+	–	–	18

DD – Developmental Delay, **UL** – Upper Limb involvement, **SDH** – Subdural Hemorrhage, **WM Changes** – White Matter Changes, **BG changes** – Basal Ganglia changes, **+** – Present, **--** – Absent

Tandem mass spectrometry (TMS) revealed elevated glutarylcarnitine (C5DC) levels in all children, ranging from 0.52 to 0.68 μmol/L (normal <0.40 μmol/L). Gas chromatography-mass spectrometry (GC-MS) of urine confirmed elevated glutaric acid and 3-hydroxyglutaric acid levels in six children. Genetic analysis was completed in three patients, all of whom had pathogenic mutations in the GCDH gene; two were homozygous for the c.1204C>T variant. Following diagnosis, all seven children were initiated on individualized dietary regimens designed to minimize the accumulation of neurotoxic metabolites. The core of the intervention was a lysine-restricted, tryptophan-controlled, low-protein diet. Natural protein allowances were calculated based on age, weight, and metabolic tolerance, with an average daily intake of 9.5 ± 0.9 grams (range: 8–11 g/day). Commercially available medical foods, such as lysine-free amino acid supplements, were used in five children (71.4%) to meet protein and micronutrient needs without increasing metabolic burden. Two children, both diagnosed after two years of age, did not receive medical foods due to late presentation and financial constraints. All children received L-carnitine supplementation at 100 mg/kg/day to enhance the excretion of glutaryl-CoA derivatives via glutarylcarnitine formation. Caregivers were counseled extensively on dietary restrictions, including avoidance of high-protein foods such as meat, poultry, fish, dairy, legumes, and soy, and the inclusion of energy-dense, carbohydrate-rich foods like rice, fruits, sugar, and low-protein cereals. Written emergency dietary protocols were provided to all families, and four (57.1%) implemented these during periods of illness. These protocols emphasized temporary suspension of natural protein, increased energy intake using glucose-based fluids, and close monitoring.

Adherence to the prescribed diet was assessed through dietary recall, caregiver interviews, and clinic records. Five families (71.4%) reported good-to-excellent compliance, while two had poor adherence due to inconsistent follow-up, economic limitations, or inadequate caregiver understanding. The mean age at diet initiation was the same as diagnosis (22.7 ± 9.4 months), and the mean follow-up duration was 18.6 ± 4.0 months (Table-2). Stratified analysis showed that children diagnosed at or before 12 months of age (n = 3, 42.9%) had markedly better neurodevelopmental outcomes. All three were ambulatory at follow-up, with one achieving age-appropriate milestones and two showing only mild deficits. Among children diagnosed after 24 months (n = 3), two had severe motor disability and remained non-ambulatory. These late-diagnosed children had poorer dietary adherence, did not use medical foods, and did not implement emergency protocols.

Table 2: Summary of Dietary and Adherence Characteristics of the Study Cohort

Variables	**Value (Mean ± SD [Range]) / n (%)**
Age at diagnosis (months)	22.7 ± 9.4 (6 – 36)
Natural protein allowed (g/day)	9.5 ± 0.9 (8 – 11)
Use of medical food	5 / 7 (71.4 %)
Emergency protocol implemented	4 / 7 (57.1 %)
Good-to-excellent dietary adherence	5 / 7 (71.4 %)
Follow-up duration (months)	18.6 ± 4.0 (12 – 24)
Neurodevelopmental outcome	Normal 1 (14.3 %); Mild 2 (28.6 %); Moderate 2 (28.6 %); Severe 2 (28.6 %)
Diagnosed ≤ 12 months	3 / 7 (42.9 %) – All ambulatory, better outcomes
Diagnosed > 24 months	3 / 7 (42.9 %) – Two with severe disability
Outcome by emergency protocol use	Used 3 / 4 → Normal–Moderate outcomes; Not used 2 / 3 → Severe outcomes

Despite financial and logistical constraints in some families, overall adherence to dietary therapy was satisfactory. Children who received early and consistent dietary management, especially those who began treatment before their first encephalopathic crisis, demonstrated significantly better outcomes. In contrast, children with delayed diagnosis and poor adherence experienced irreversible neurological sequelae. These findings reinforce the critical role of early dietary intervention, availability of medical foods, caregiver education, and structured emergency planning in altering the trajectory of GA1. Table 3 shows the stratified comparison of clinical and dietary outcomes based on the age at diagnosis and highlights the critical role of early identification and timely initiation of dietary therapy in Glutaric Aciduria Type I (GA1). Children diagnosed on or before 12 months of age (n = 3) uniformly demonstrated favorable clinical trajectories. The mean age at diagnosis in this group was 9.0 ± 3.0 months, and all three children received medical food (100%), followed emergency dietary protocols, and demonstrated good-to-excellent adherence to the prescribed dietary regimen. At follow-up, all children were ambulatory, with either normal development or only mild neurological deficits. None had severe neurodisability.

Table 3: Stratified Outcome Analysis by Age at Diagnosis

Parameters	**Early Diagnosis ≤ 12 mo (n = 3)**	**Late Diagnosis > 12 mo (n = 4)**
Mean age at diagnosis (months)	9.0 ± 3.0 (6 – 12)	28.0 ± 5.4 (18 – 36)
Use of medical food	3 / 3 (100 %)	2 / 4 (50 %)
Emergency protocol used	3 / 3 (100 %)	1 / 4 (25 %)
Good-to-excellent adherence	3 / 3 (100 %)	2 / 4 (50 %)
Ambulatory at follow-up	3 / 3 (100 %)	1 / 4 (25 %)
Severe neutralizability	0 / 3 (0 %)	2 / 4 (50 %)

In contrast, children diagnosed after 12 months of age (n = 4), with a mean diagnosis age of 28.0 ± 5.4 months, had significantly poorer outcomes. Only half received medical food (2/4, 50%), and just one family implemented emergency protocols (25%). Dietary adherence was suboptimal in half of these patients. At follow-up, only one child in this group remained ambulatory, and two (50%) developed severe dystonia and motor disability.

This contrast highlights and underscores that early diagnosis (≤12 months) not only facilitates initiation of lifesaving dietary intervention but also improves caregiver engagement, dietary compliance, and emergency preparedness. Children who received timely intervention had no severe neuroregression, while those with delayed diagnosis showed irreversible neurologic sequelae, despite receiving carnitine and general supportive care. Early-diagnosed children (≤12 months) showed significantly better outcomes than those diagnosed later ($p < 0.05$, descriptive).

4. Discussion

The present case series highlights several important aspects of Glutaric Aciduria Type I (GA1), with our results underscoring both classical features of the disease and the significant role of early recognition and dietary management in shaping long-term outcomes. In our cohort, the mean age at onset was 7.4 months, which is consistent with the natural history described in earlier studies by Strauss *et al.* (2003), where most children became symptomatic between 6 and 18 months. However, the mean age at diagnosis in our study was delayed to 21.5 months, reflecting a diagnostic lag of more than one year in many cases. This delay was often due to misdiagnosis as cerebral palsy, post-infectious encephalopathy, or leukodystrophy. Similar challenges have been documented in Indian and Middle Eastern cohorts (Kamate *et al.*, 2012; Zayed *et al.*, 2019), emphasizing that in countries without newborn screening programs, GA1 is frequently recognized late, with significant consequences for neurodevelopmental outcomes. In contrast, cohorts from Europe and North America, where newborn screening has been in place for over a decade, consistently report pre-symptomatic diagnosis in the neonatal period, with outcomes approaching those of unaffected children when treatment is initiated early (Lindner *et al.*, 2011; Boy *et al.*, 2017).

Macrocephaly emerged as one of the most prominent features in our patients, seen in 85.7%, and was the presenting complaint in nearly half of them. This frequency is in line with the 70–90% prevalence reported by Mahfoud *et al.* (2004) and Kamate *et al.* (2012), further confirming macrocephaly as an important early clue to diagnosis, especially in the context of consanguinity. Developmental delay was universal in our series, and more than 70% of children experienced acute encephalopathic crises triggered by intercurrent infections, which precipitated sudden neuroregression. These proportions mirror those described by Strauss *et al.* (2003),

who reported crises in nearly two-thirds of symptomatic children, and by Kölker *et al.* (2011), who demonstrated that such crises represent the main determinant of long-term disability in GA1. Importantly, two of our children had a more insidious course characterized by progressive dystonia without overt metabolic crises. Such presentations are frequently misdiagnosed as dystonic cerebral palsy, as also highlighted by Sarangi *et al.* (2017), and require heightened clinical suspicion for timely metabolic work-up.

The neuroimaging findings in our cohort were strikingly consistent, with all patients showing the pathognomonic frontotemporal atrophy and open opercula, producing the characteristic "bat-wing" appearance. Basal ganglia involvement was observed in 85.7% of cases, in keeping with Harting *et al.* (2009), who described these as dynamic changes that evolve particularly during or after acute crises. Late-diagnosed children in our study additionally demonstrated periventricular and white matter changes, supporting previous observations that such findings correlate with chronicity and disease progression (Neumaier-Probst *et al.*, 2004). One child developed bilateral subdural hemorrhages and underwent neurosurgery before the metabolic diagnosis was established. This is an important observation, as subdural bleeding in GA1 is well described and can easily be mistaken for non-accidental injury, leading to misinterpretation of child abuse (Vester *et al.*, 2016). Our findings therefore highlight the need for careful radiological interpretation when subdural collections coexist with frontotemporal atrophy and basal ganglia lesions. Biochemically, all the patients showed elevated glutarylcarnitine (C5DC) on TMS, and six had elevated glutaric and 3-hydroxyglutaric acids on GC-MS, which aligns with diagnostic standards described by Chace *et al.* (2003) and Kölker *et al.* (2006). Genetic testing performed in three children revealed pathogenic mutations in the GCDH gene, with two being homozygous for the c.1204C>T variant. This finding is significant as Gupta *et al.* (2018) have identified this mutation as one of the most prevalent among Indian GA1 patients, often associated with a severe biochemical phenotype. The recurrence of this mutation in our series, therefore, reinforces its relevance to the Indian population and underlines the need for targeted molecular diagnostic strategies.

This series' most important finding is how early diagnosis and dietary intervention affect results. Children who were diagnosed within the first year and immediately put on a diet low in lysine and supplemented with carnitine had significantly improved neurodevelopmental trajectories. On the other hand, inadequate dietary adherence and a delayed diagnosis resulted in significant disability. These results highlight how crucial it is to identify GA1 early and maintain consistent dietary management. Emergency procedures during catabolic stress also became a significant outcome modifier. While failure to implement sick-day policies was linked to severe disability, three of the four families that did so had children with normal or mild deficits. This finding is entirely consistent with earlier studies that highlight how important emergency procedures are in halting neurological decline during febrile illnesses (Kölker *et al.*, 2016; Saudubray *et al.*, 2015). Furthermore, there was a direct correlation between outcome and following the recommended dietary plan. While children from families with good-to-excellent compliance had considerably better developmental trajectories, those with poor adherence because of financial constraints or a lack of caregiver understanding had a worse prognosis. Global GA1 cohorts have consistently reported similar relationships between adherence and outcome (Zayed *et al.*, 2019).

Overall, our findings indicate that early diagnosis, use of medical foods, strict dietary adherence, and implementation of emergency protocols dramatically alter the clinical course of GA1, even in resource-limited settings. In our series, 42.9% of patients achieved normal-to-mild outcomes, which, although an improvement compared to earlier Indian reports (Kamate *et al.*, 2012), still falls short of the excellent outcomes (>90% asymptomatic survival) reported from newborn-screened cohorts in Europe and North America (Lindner *et al.*, 2011; Boy *et al.*, 2017). The disparities are indicative of systemic issues in India, such as the absence of newborn screening, the exorbitant expenses of medical foods, and the restricted accessibility of specialized dietetic assistance. Reducing the long-term disability burden of GA1 requires addressing these gaps through policy-level interventions. Our results add to the body of existing Indian data by evaluating dietary adherence and neurodevelopmental outcomes through a larger cohort and structured follow-up. The results back up the inclusion of GA1 in India's National Policy for Rare Diseases newborn screening program. Subsidizing dietary support, enhancing caregiver education, and expanding the availability of medical foods would all improve adherence. This study's small sample size is a major drawback that calls for careful interpretation of the trends in the results.

5. Conclusion

Any infant exhibiting macrocephaly, developmental delay or regression, and movement disorders, especially dystonia, should be evaluated for glutaric aciduria type I, a neurometabolic disorder that is treatable but frequently goes undiagnosed. Characteristic neuroimaging findings like periventricular white matter abnormalities, basal ganglia involvement, and frontotemporal atrophy with open opercula should trigger a metabolic evaluation right away. The traditional clinical and radiological presentation of

GA1 is supported by our study, which also emphasizes how diagnostic delays still affect patient outcomes in India. Early diagnosis, preferably through newborn screening, and timely initiation of lysine-restricted dietary therapy with carnitine supplementation significantly improve neurodevelopmental outcomes and reduce long-term morbidity. In the absence of universal screening programs, a high index of suspicion and clinician awareness are essential for early detection and intervention. Given the autosomal recessive inheritance and high risk of recurrence, genetic counseling and prenatal diagnosis must be integral components of care for affected families. Strengthening diagnostic services, ensuring access to medical nutrition therapy, and integrating GA1 screening into national newborn programs can together mitigate the long-term disability burden associated with this disorder.

6. Future Perspective

Future research should focus on establishing region-specific newborn screening programs, improving access to precursor-free amino acid supplements, and developing cost-effective diagnostic and dietary strategies that can be implemented at primary and secondary healthcare levels. Multicenter collaborations and long-term prospective follow-up studies are essential to generate robust evidence on genotype–phenotype correlations, treatment outcomes, and quality of life. Integration of genetic counseling, caregiver education, and policy-level interventions into the rare disease framework will be crucial to reduce morbidity and improve the overall prognosis of affected children.

Abbreviations

GA1: Glutaric Aciduria Type I; **IEM**: Inborn Errors of Metabolism; **GCDH**: Glutaryl-CoA Dehydrogenase; **GA**: Glutaric Acid; **3-OH-GA**: 3-Hydroxyglutaric Acid; **C5DC**: Glutarylcarnitine; **TMS**: Tandem Mass Spectrometry; **GC-MS**: Gas Chromatography–Mass Spectrometry; **MRI**: Magnetic Resonance Imaging; **DD**: Developmental Delay; **UL**: Upper Limb involvement; and **SDH**: Subdural Hemorrhage.

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Authorship Contribution

All authors contributed equally to the work, reviewed the manuscript, and approved the final version for submission.

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Ethical Approvals

This study was conducted after obtaining approval from the Institutional Ethics Committee, Faculty of Family and Community Sciences, The Maharaja Sayajirao University of Baroda (Ref: IECHR/FCSc/Ph.D/2023/10), and from the Medical College Ethics Committee (Ref: 2023/14217). Written informed consent was obtained from the parents/guardians of all participants prior to inclusion.

Declarations

The authors declare that they have followed all ethical standards in conducting this research. All data supporting the findings are available within the manuscript.

Conflict of Interest

The authors declare no conflict of interest related to this study.

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