DOI: 10.7860/JCDR/2026/77493.22188

Case Report

Paediatrics Section

Short-chain Acyl-CoA Dehydrogenase Deficiency in a Child: A Case Report

SANJAY CHAVAN[1], SADHU POOJA[2], SURESHA[3], SARNYA VERMA[4], SHAILAJA MANE[5]

ABSTRACT

Short-chain 3-Hydroxyacyl-CoA Dehydrogenase (SCHAD) enzyme deficiency is an autosomal recessive inborn error of metabolism affecting mitochondrial Fatty Acid Oxidation (FAO). In this condition, the body fails to produce energy from fats during times of stress. Effective energy production relies on the mitochondrial β-oxidation of fatty acids, which is especially crucial during periods of fasting, infections, and other metabolic stressors. Children with this deficiency often present with transient and nonspecific symptoms. Here, we present the case of a five-year-old male child with a recurrent history of seizures, persistent hypoglycaemia, metabolic acidosis with hypotension requiring inotropic support, and a deteriorating Glasgow Coma Scale score necessitating mechanical ventilation. Upon evaluation, he was found to have hypoinsulinemia, and his electroencephalogram suggested encephalopathy. After ruling out sepsis, hyperinsulinaemia, and meningoencephalitis, inborn errors of metabolism were suspected, with a fatty acid oxidation defect being the most likely diagnosis. The patient was ultimately diagnosed with SCHAD deficiency using Gas Chromatography-Mass Spectrometry Tandem Mass Spectrometry (GCMS-TMS). The potential for rapid deterioration associated with SCHAD deficiency underscores the need for prompt evaluation and intervention, which are essential for early diagnosis and favourable outcomes to prevent morbidity and mortality. The serious complications associated with this condition also highlight the necessity for newborn screening for inborn errors of metabolism.

Keywords: Hyperinsulinaemia, Hypoglycaemia, Inborn errors of metabolism, Mitochondrial fatty acid oxidation, Paediatric seizures

CASE REPORT

A five-year-old male child, the third born in a non consanguineous marriage, presented with a normal birth history, age-appropriate development, and good nourishment, exhibiting a normal appetite. He was brought to the pediatric emergency department of a tertiary care hospital with complaints of sudden onset high-grade intermittent fever and non projectile vomiting (8-10 episodes over three days), along with multiple episodes of generalised tonic-clonic seizures with eyes rolling upward lasting 5-6 minutes within the last 24 hours. The patient had a history of loss of consciousness lasting five minutes and one episode of vomiting six months ago. Additionally, he experienced fever, vomiting, and a generalised tonic-clonic seizure one year ago, for which he was admitted and treated as a simple febrile seizure. At that time, he was not started on any antiseizure medication, as it was considered only a simple febrile seizure, and clobazam prophylaxis had been advised. There was no family history of seizures or similar complaints, and the child had received only the birth dose of his vaccinations.

Upon presentation, the patient was found to be drowsy with poor respiratory effort, exhibiting a respiratory rate of 18 cycles per minute and oxygen saturation of 84% on room air. He had low volume pulses and a blood pressure of 76/46 mmHg. His Random Blood Sugar (RBS) level was 20 mg/dL. He was promptly started on intravenous normal saline and D10 boluses, after which his RBS improved to 86 mg/dL. However, he then experienced two additional episodes of generalised tonic-clonic seizures, each lasting 6-7 minutes, for which he was loaded with levetiracetam at a dosage of 20 mg/kg. The patient continued to deteriorate, resulting in a low Glasgow Coma Scale score of 8/15, necessitating intubation and mechanical ventilation. He was subsequently transferred to the pediatric Intensive Care Unit (ICU).

Sepsis was ruled out after obtaining negative results from blood, urine, and cerebrospinal fluid tests. Upon evaluation, the patient exhibited low serum insulin levels, confirming hypoinsulinemia and ruling out hyperinsulinaemia. Arterial Blood Gas (ABG) analysis indicated metabolic acidosis (pH of 7.23, bicarbonate 5.9, and Pco2 14), for which bicarbonate correction was administered. Urine tests for ketones and reducing substances returned positive results [Table/Fig-1]. The child also displayed low magnesium and vitamin D levels, which were corrected with Injection Magnesium Sulfate at a dosage of 50 mg/kg/day for three days and Cholecalciferol 60,000 IU per week for six doses. Despite these interventions, the patient continued to experience persistent metabolic acidosis, requiring multiple bicarbonate corrections.

Lab investigations	Value	Reference range
Haemoglobin	13.7 gm/dL	12-14 gm/dL
Total leucocyte count	26240/mcL	4000-9500/mcL
Neutrophil	86%	
Lymphocyte	9%	
Platelet	4.09 lacs/mcL	1.5-4.1 lacs/mcL
Uric acid	11.8 mg/dL	3.5-7.2 mg/dL
Ammonia	249 mcg/dL	20-120 mcg/dL
Lactate	2.53 mg/mL	3.6-18 mg/dL
RBS	20 mg/dL	70-150 mg/dL
Serum insulin	2.5 uIU/mL	15-150uIU/mL
Serum cortisol	61.6 mcg/dL	3-21 mcg/dL
Serum magnesium	1.50	1.80-2.40 mg/dL
Serum calcium	7.90 mg/dL	8.8-10.8 mg/dL
25-OH vitamin D	8.90 ng/mL	<10 ng/mL- severe deficiency
Blood culture	No growth of microorganisms	
Urine for ketones and reducing substance	Positive	

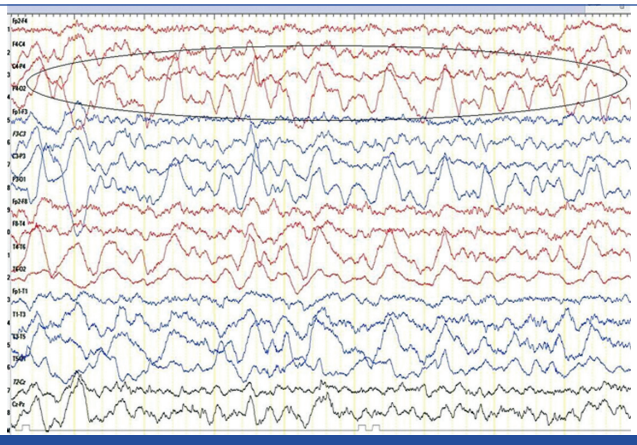
[Table/Fig-1]: Blood and urine investigations.

Intravenous antibiotics were initiated, including Injection Ceftriaxone at 100 mg/kg/day and Injection Vancomycin at 20 mg/kg every six hours, along with antiviral medication, Injection Acyclovir at 60 mg/kg/day, administered for 14 days due to suspected acute encephalitis syndrome. The patient also displayed hypotensive readings, which necessitated the initiation of intravenous adrenaline infusion. After ruling out hyperinsulinaemia and acute encephalitis syndrome, samples were sent for GCMS-TMS analysis, and the patient was started on intravenous carnitine at 100 mg/kg/day, oral biotin at 20 mg/day, Vitamin B12 at 1 mg/day, and Coenzyme Q supplements at 10 mg/kg/day (the metabolic cocktail), suspecting an inborn error of metabolism.

Routine microscopy and culture of the cerebrospinal fluid did not indicate any infectious etiology [Table/Fig-2], which ruled out meningoencephalitis. The patient continued to experience multiple seizure episodes, leading to the administration of injection phenytoin at a loading dose of 20 mg/kg and a maintenance dose of 5 mg/kg/day. The patient was extubated one week later and gradually weaned off oxygen support. The electroencephalogram showed high-amplitude delta waves, suggestive of encephalopathy [Table/Fig-3]. An Magnetic Resonance Imaging (MRI) of the brain, both plain and with contrast, revealed mild diffusion restriction on Diffusion Weighted Imaging (DWI) and hyperintense signals on T2-weighted images [Table/Fig-4,5].

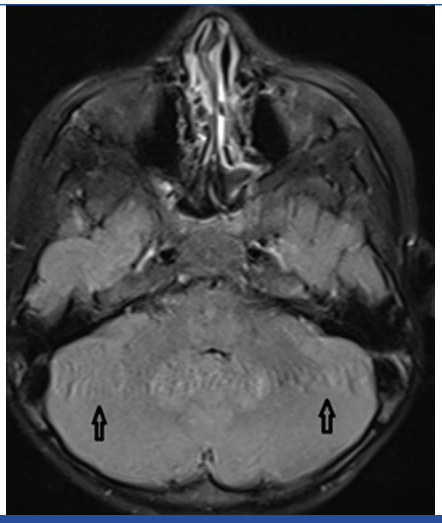
Cerebrospinal fluid analysis	Value	Normal range
Cobweb	Absent	Absent
Deposits	Absent	Absent
Total leucocyte count	2/cu.mm	0-10/cu.mm
Lymphocytes	100%	
Proteins	155.40 mg/dL	15-45 mg/dL
Glucose	43 mg/dL	40-80 mg/dL
Adenosine deaminase	<0.5	0-5u/ltr
Cerebrospinal fluid culture	No growth of microorganisms	

[Table/Fig-2]: CSF analysis.

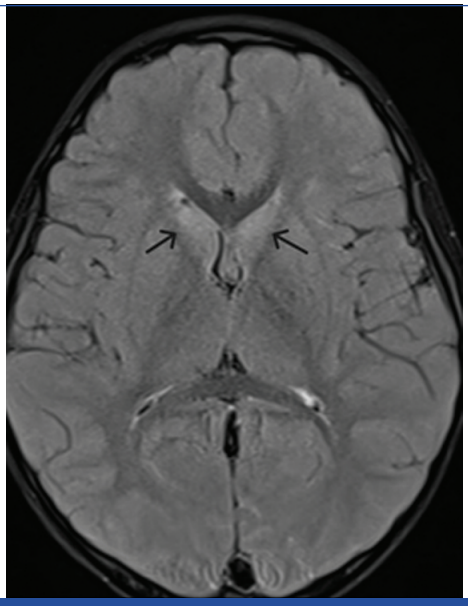


[Table/Fig-3]: EEG showing high amplitude delta waves.

Due to recurrent seizures and hypoglycaemia associated with persistent metabolic acidosis, further evaluation for inborn errors of metabolism was conducted; the GCMS-TMS study ultimately revealed SCHAD [Table/Fig-6]. The parents were counseled regarding whole-exome sequencing, which could not be performed due to financial constraints. The patient was discharged on levetiracetam at a dosage of 40 mg/kg/day, phenytoin at 5 mg/kg/day, and a metabolic cocktail. The parents were counseled regarding dietary and lifestyle modifications as well as the importance of regular follow-up. One month postdischarge, during a follow-up appointment, the child was seizure free and had no further episodes of hypoglycaemia. Consequently, he was advised to taper phenytoin to 2.5 mg/kg/day for one week, with the plan to discontinue phenytoin altogether if he remained seizure free.



[Table/Fig-4]: MRI (Brain)- Bilateral cerebellar hemispheres involving dentate nuclei showing mild diffusion restriction on DW1.



[Table/Fig-5]: MRI (Brain)- hyperintense signal in bilateral frontal periventricular white matter on T2.

Analytes		Observed value (µmol/L)	Reference range (µmol/L)
Amino acid analytes	Alanine	698.44	74-613
	Valine	247.37	41-233
	Leucine-isoleucine	271.79	26-250
	Methionine	70.11	1-54
	Tyrosine	398.58	17-250
ACYL carnitine analytes	Malonylcarnitine+3-OH-Butyrylcarnitine (C3-DC+C4- OH)	2.52	<0.45

Fatty Acid Oxidation (FAO) defect screening	Disorder	Result
	Short Chain 3- Hydroxy acyl-CoA Dehydrogenase (SCHAD) deficiency	Abnormal
Result and interpretation	Amino acid profile	Abnormal
	Acylcarnitine profile	Abnormal
Result: Screen positive		

[Table/Fig-6]: TMS report.

DISCUSSION

The SCHAD deficiency is a rare metabolic autosomal recessive disorder affecting the β-oxidation of fatty acids, caused by loss-of-function mutations in the Hydroxy Acyl-CoA Dehydrogenase (HADH) gene [1]. The SCHAD enzyme, which is found in the mitochondrial matrix, is encoded by the HADH gene located on

chromosome 4q22-q26 [1]. The conversion of L-3-hydroxyacyl-CoA to 3-ketoacyl-CoA is catalysed by Medium-chain 3-Hydroxy Acyl-CoA Dehydrogenase (MCHAD) and SCHAD, both of which are nicotinamide adenine dinucleotide (NAD+)-dependent enzymes [2]. SCHAD is highly expressed in pancreatic beta cells and is also present in lymphoblasts, adipocytes, and kidney tissue [3]. This enzyme catalyses the third step of fatty acid degradation [4]. SCHAD was first isolated from rat liver and later cloned from human brain tissue [5].

Mitochondrial Fatty Acid Oxidation (FAO) is crucial for producing Adenosine Triphosphate (ATP) when the body demands more energy due to conditions such as hunger, fever, or increased muscle activity [6]. Through a series of cyclic steps, fatty acids are oxidised to yield acyl-CoA and acetyl-CoA [2]. Acetyl-CoA serves as a direct metabolic fuel in tissues, including the heart and skeletal muscles, and is also a substrate for ketogenesis in the liver [6]. The acetyl-CoA intermediates with shorter chains re-enter the cycle until they undergo complete degradation. Numerous FAO steps related to genetic abnormalities have been thoroughly described at the biochemical and molecular levels, leading to the development of metabolic indicators for newborn screening in the population [6].

FAO defects can produce a wide variety of symptoms at any age, which may include skeletal myopathy, cardiomyopathy, liver failure, hepatic encephalopathy, and sudden infant death. Hepatic ketogenesis failure can also lead to hypoketotic hypoglycaemia [9]. In cases of HADH deficiency, hyperinsulinaemia is also associated with hypoketotic hypoglycaemia. Elevated levels of medium-chain dicarboxylic acids, 3-hydroxydicarboxylic metabolites, and 3-hydroxyglutarate are noted from the urinary organic acid profile. Plasma acylcarnitine analysis typically shows increased Hydroxybutyrylcarnitine (C4-OH). A decreased activity of C4-hydroxyacyl-CoA dehydrogenase in fibroblasts, lymphocytes, and tissues, along with the demonstration of HADH gene mutations, confirms the diagnosis [9].

In patients with SCHAD deficiency and hyperinsulinism, diazoxide is recommended as a treatment [10]. Diazoxide activates KATP (ATP-sensitive potassium) channels, which remain unaffected in SCHAD patients, making it helpful in controlling hypoglycemic episodes [3]. In the non-hyperinsulinemic form of SCHAD deficiency, prevention of fasting is advised, as there is a lack of evidence regarding other treatment modalities [10]. A comparison of the findings in the present study with contrasting studies is shown in [Table/Fig-7] [1,6,7,9,11,12].

Authors name (Ref. No.)	Place/year of the study	Age/gender	Findings/symptoms	Conclusion
Popa FI et al., [1]	Italy/2012	Not specified	Hyper insulinemic hypoketotic hypoglycaemia, altered organic acids and acylcarnitine's	Identified a novel mutation in SCHAD gene causing hyper insulinemic hypoglycaemia and metabolic disturbances. Management with metabolic interventions is essential.
Bennett MJ et al., [6]	USA/2006	Not specified	Reye-like syndrome, vomiting, lethargy, liver dysfunction	Identified novel mutations in SCHAD gene causing Reye-like syndrome. Immediate treatment with glucose and supportive care is needed during crises.
Repic Lampret B et al., [7]	Biochemia Medica/2015	Not specified/ male child	Hypoglycaemia, failure to thrive	SCHAD deficiency confirmed by genetic analysis. Managed with dietary interventions and metabolic support.
Martins E et al., [9]	Not specified/2011	Not specified	Clinical symptoms include hypoglycaemia, elevated acylcarnitine levels, and organic acid disturbances. All patients had variable severity of symptoms, some presenting with failure to thrive or developmental delay	Early diagnosis is crucial for managing the disease effectively. The report of four new cases emphasises the importance of considering SCHAD deficiency in cases of unexplained hypoglycaemia. Early treatment and metabolic management are key to improving outcomes.
Mohammadi M et al., [11]	Iran/2013	15-year-old/ Not specified	Respiratory distress and loss of consciousness with intermittent vomiting and early fatigue with normal activity for 2 years	Symptoms of metabolic disease can be seen with delay in infants with normal development. Because of the low recognition of symptoms particularly cardiac involvement, delay in diagnosis can be life threatening.
Clayton PT et al., [12]	London, United Kingdom/2001	19 months/ Female	Hypoglycaemic convulsions, hypoketotic hypoglycaemia, poor appetite Elevated plasma insulin concentrations, elevated blood spot hydroxybutyrylcarnitine	Identified a homozygous C773T mutation in the SCHAD gene, leading to hyperinsulinism. This is the first time fatty acid β-oxidation defect has been linked to hyperinsulinism. The condition was controlled with diazoxide and chlorothiazide.

[Table/Fig-7]: Comparison of multiple studies on SCHAD deficiency [1,6,7,9,11,12].

The mitochondrial short-chain β-oxidation pathway is catalysed by the SCHAD enzyme, which dehydrogenates C4 and C6 fatty acids. Due to impaired SCHAD function, butyryl carnitine (C4-carnitine), butyryl glycine, ethylmalonic acid, and methyl succinic acid accumulate in the blood and urine. It is important to note that two other hereditary disorders, Isobutyryl-CoA Dehydrogenase (IBD) deficiency and ethylmalonic encephalopathy, can also result from the accumulation of C4-carnitine, specifically four-carbon carnitine esters [7].

A Dutch retrospective study reported a prevalence of 1 in 50,000 at birth, with most cases presenting around three years of age [8]. This disorder can affect individuals of all ages, including adults, children, and newborns. Due to extensive diagnostic evaluations conducted on children with nonspecific symptoms such as developmental delay, failure to thrive, and myopathy, most cases of SCHAD deficiency have been identified [7]. Genome-wide association studies have found genetic variations linked to relative amounts of C4-carnitine. Additionally, several proteomic investigations are underway to identify biomarkers that can help distinguish asymptomatic individuals with SCHAD deficiency from those at risk of developing symptoms [7].

CONCLUSION(S)

This case emphasises the necessity of considering inborn errors of metabolism, such as SCHAD deficiency, in pediatric patients presenting with recurrent episodes of seizures, hypoglycaemia, persistent metabolic acidosis, and a variety of nonspecific symptoms. Early recognition and intervention, prevention of metabolic stressors, and symptomatic management- including the prevention of seizures and hypoglycaemia- are crucial for improving long-term outcomes. However, further studies are needed to explore the association between SCHAD deficiency and neurodevelopmental outcomes and prognosis.

REFERENCES

[1] Popa FI, Perlini S, Teofoli F, Degani D, Funghini S, La Marca G, et al. 3-hydroxyacyl-coenzyme a dehydrogenase deficiency: Identification of a new mutation causing hyperinsulinemic hypoketotic hypoglycemia, altered organic acids and acylcarnitines concentrations. JIMD Rep. 2012:2:71-77.
[2] Schulz N, Himmelbauer H, Rath M, van Weeghel M, Houten S, Kulik W, et al. Role of medium-and short-chain L-3-hydroxyacyl-CoA dehydrogenase in the regulation of body weight and thermogenesis. Endocrinology. 2011;152(12):4641-51.
[3] Zhang W, Sang YM. Genetic pathogenesis, diagnosis, and treatment of short-chain 3-hydroxyacyl-coenzyme A dehydrogenase hyperinsulinism. Orphanet J Rare Dis. 2021;16:467. Available from: https://doi.org/10.1186/s13023-021-02088-6.

[4] St-Louis JL, El Jellas K, Velasco K, Slipp BA, Hu J, Helgeland G, et al. Deficiency of the metabolic enzyme SCHAD in pancreatic β-cells promotes amino acid-sensitive hypoglycemia. J Biol Chem. 2023;299(8):104986. Doi: 10.1016/j.jbc.2023.104986. Epub 2023 Jun 29. PMID: 37392854; PMCID: PMC10407745.
[5] Yang SY, He XY, Schulz H. 3-Hydroxyacyl-CoA dehydrogenase and short chain 3-hydroxyacyl-CoA dehydrogenase in human health and disease. FEBS J. 2005;272(19):4874-83. Doi: 10.1111/j.1742-4658.2005.04911.x. PMID: 16176262.
[6] Bennett MJ, Russell LK, Tokunaga C, Narayan SB, Tan L, Seegmiller A, et al. Reye-like syndrome resulting from novel missense mutations in mitochondrial medium- and short-chain l-3-hydroxy-acyl-CoA dehydrogenase. Molecular Genetics and Metabolism. 2006;89(1-2):74-79.
[7] Repic Lampret B, Murko S, Debeljak M, Zerjav Tansek M, Fister P, Battelino T. A case report of short-chain acyl-CoA dehydrogenase deficiency (SCADD). Biochemia Medica. 2015;25(2):279-84.
[8] van Maldegem BT, Duran M, Wanders RJ, Niezen-Koning KE, Hogeveen M, Ijlst L, et al. Clinical, biochemical, and genetic heterogeneity in short-chain acyl-coenzyme A dehydrogenase deficiency. JAMA. 2006;296(8):943-52.
[9] Martins E, Cardoso ML, Rodrigues E, Barbot C, Ramos A, Bennett MJ et al. Short-chain 3-hydroxyacyl-CoA dehydrogenase deficiency: The clinical relevance of an early diagnosis and report of four new cases. J Inherit Metab Dis. 2011;34(3):835-42. Doi: 10.1007/s10545-011-9287-7.
[10] Kliegman RM, St Geme JW, Blum NJ, Tasker RC, Wilson KM, Schuh AM, et al. Pediatric infectious diseases. In: Kliegman RM, St Geme JW, Blum NJ, Tasker RC, Wilson KM, et al, editors. Nelson Textbook of Pediatrics. 22nd ed. Philadelphia: Elsevier; 2025. p. 859-897.e2.
[11] Mohammadi M, Alijanpour M, Khodabakhsh E, Rezapour M. A rare case with short chain Hydroxyacyl-CoA Dehydrogenase Deficiency (SCHAD) with symptom of cardiac involvement. J Babol Univ Med Sci. 2013;15(4):115-19.
[12] Clayton PT, Eaton S, Aynsley-Green A, Edginton M, Hussain K, Krywawych S, et al. Hyperinsulinism in short-chain L-3-hydroxyacyl-CoA dehydrogenase deficiency reveals the importance of β-oxidation in insulin secretion. J Clin Invest. 2001;108(3):457-65. Available from: https://doi.org/10.1172/JCI11294.

PARTICULARS OF CONTRIBUTORS:
1. Professor, Department of Paediatrics, Dr. D. Y. Patil Medical College, Hospital and Research Centre, Dr. D. Y. Patil Vidyapeeth, Pune, Maharashtra, India.
2. Resident, Department of Paediatrics, Dr. D. Y. Patil Medical College, Hospital and Research Centre, Dr. D. Y. Patil Vidyapeeth, Pune, Maharashtra, India.
3. Resident, Department of Paediatrics, Dr. D. Y. Patil Medical College, Hospital and Research Centre, Dr. D. Y. Patil Vidyapeeth, Pune, Maharashtra, India.
4. Resident, Department of Paediatrics, Dr. D. Y. Patil Medical College, Hospital and Research Centre, Dr. D. Y. Patil Vidyapeeth, Pune, Maharashtra, India.
5. Professor and Head, Department of Paediatrics, Dr. D. Y. Patil Medical College, Hospital and Research Centre, Dr. D. Y. Patil Vidyapeeth, Pune, Maharashtra, India.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:
Suresha,
Resident, Department of Paediatrics, Dr. D. Y. Patil Medical College, Hospital and Research Centre, Pimpri, Pune-411018, Maharashtra, India.
E-mail: sureshld000@gmail.com

PLAGIARISM CHECKING METHODS: [Jain H et al.]
- Plagiarism X-checker: Feb 07, 2025
- Manual Googling: Apr 12, 2025
- iThenticate Software: Apr 14, 2025 (5%)

ETYMOLOGY: Author Origin

EMENDATIONS: 7

AUTHOR DECLARATION:
- Financial or Other Competing Interests: None
- Was informed consent obtained from the subjects involved in the study? Yes
- For any images presented appropriate consent has been obtained from the subjects. Yes

Date of Submission: **Jan 28, 2025**
Date of Peer Review: **Mar 10, 2025**
Date of Acceptance: **Apr 16, 2025**
Date of Publishing: **Jan 01, 2026**