



ORIGINAL RESEARCH PAPER

Endocrinology

CLINICAL, BIOCHEMICAL AND ETIOLOGICAL CHARACTERISTICS OF HYPOGLYCEMIA IN CHILDREN

KEY WORDS:

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ABSTRACT

Background: Pediatric hypoglycemia is a common but potentially fatal metabolic emergency with a variety of causes ranging from brief physiological conditions to complex endocrine and metabolic diseases. Systematic examination of clinical presentation and biochemical trends aids in early etiological diagnosis and prevention of neurodevelopmental consequences. **Objectives:** To examine the clinical profile, biochemical parameters, etiological spectrum, and outcomes of children presenting with hypoglycemia in a tertiary care facility. **Methods:** This is an observational case series of pediatric children who had documented hypoglycemia. Demographic information, clinical characteristics, anthropometry, and biochemical data collected during the crucial sample, final diagnosis, and treatment were examined. The study comprised of twenty children. The most common cause was hyperinsulinemic hypoglycemia, which was followed by endocrine deficits, ketotic hypoglycemia, and inborn metabolic abnormalities. Each etiology produced distinct biochemical patterns. **Conclusion:** Careful interpretation of crucial samples, together with clinical context, enables early etiological categorization of pediatric hypoglycemia, guiding focused therapy and improving outcomes.

INTRODUCTION

Hypoglycemia in children has several unique characteristics in terms of diagnosis and treatment, which are mostly due to age-related changes in glucose homeostasis and a wide range of reasons. While it is common but difficult to detect in newborns, it is less prevalent in neonates and toddlers, and even rarer in older children [1]. Hypoglycemia is a common metabolic-endocrine emergency in childhood, with the potential to cause lasting brain damage. As a result, it is critical to recognize and treat as soon as possible. It is critical to conduct a thorough investigation of its specific etiology in order to provide proper and targeted therapy [2].

DEFINITION OF HYPOGLYCEMIA

Neonates under 48 hours of life have plasma glucose level threshold of 47 mg/dl according to the American Academy of Pediatrics [3], and 50 mg/dl according to the Pediatric Endocrine Society [4]. Neonates over 48 hours of life, newborns, and young toddlers that are unable to communicate Hypoglycemia is defined as a plasma glucose level below 50-70 mg/dL [5]. For older children who can describe their symptoms, Whipple's triad may be used. When compared to infants, this age group exhibits more specific symptoms.

CLINICAL FEATURES

Hypoglycemic symptoms vary with age and plasma glucose levels and can be characterized as neuroglycopenic or neurogenic. Neuroglycopenic symptoms (PG <30 mg/dL) in neonates and infants can cause poor feeding, lethargy, convulsions, and coma, while older children may experience confusion, drowsiness, or loss of consciousness. Autonomic activation causes neurogenic symptoms at PG levels below 55-65 mg/dL. Jitteriness, pallor, sweating, irritability, and tachypnea are common symptoms in newborns and infants. Tremors, palpitations, sweating, hunger, anxiety, and anxiousness are common symptoms in older children. [6]

Causes of Pediatric Hypoglycemia

The causes of pediatric hypoglycemia differ depending on age and underlying illness. Neonatal reasons include transitional hypoglycemia, diabetic mothers' infants, preterm, intrauterine growth restriction, and perinatal stress. Persistent newborn hypoglycemia is most usually caused by congenital hyperinsulinism, followed by endocrine abnormalities such as cortisol or growth hormone insufficiency, and inborn metabolic defects. Ketotic hypoglycemia is the most common cause in newborns and young children, and it is usually caused by extended fasting

or an underlying illness [7]. Hyperinsulinemic hypoglycemia, both congenital and acquired, is caused by insufficient insulin secretion along with inhibited ketogenesis. Endocrine diseases, such as hypopituitarism, growth hormone deficiency, and adrenal insufficiency, decrease counter-regulatory hormone responses and are associated with hypoglycemia [8]. Inborn metabolic mistakes, such as glycogen storage diseases, fatty acid oxidation deficiencies, and gluconeogenic disorders (e.g., fructose-1,6-bisphosphatase deficiency), can occur at any age and are frequently accompanied with recurrent hypoglycemia, hepatomegaly, lactic acidosis, or hyperammonemia. Systemic disorders such as sepsis, hepatic failure, renal dysfunction, and drug-related causes are also factors [7].

DIAGNOSIS

Critical sample at the time of hypoglycemia in children is required for etiological diagnosis. When plasma glucose is <50-60 mg/dL, insulin (detectable), C-peptide (≥ 0.5 ng/mL), suppressed ketones (<0.6 mmol/L), and low free fatty acids (<1.5 mmol/L) indicate hyperinsulinemic hypoglycemia. Elevated ketones indicate proper counter-regulation. Cortisol levels (<18 μ g/dL) and growth hormone levels (<10 ng/mL) indicate endocrine inadequacies, while increased lactate or ammonia levels indicate metabolic abnormalities. Failure to collect a critical sample frequently causes delays in diagnosis and targeted care. [9]

MANAGEMENT

Low plasma glucose levels are common in the first 48 hours of life due to physiological adaptation, but persistence after this time suggests pathological hypoglycemia. Hypoglycemia lasting more than 48 hours, particularly for more than 7 days or needing glucose infusion rates more than 10 mg/kg/min, increases the risk of chronic illness [10]. Diabetic newborns and LGA infants should be examined for 12 hours, but SGA and preterm neonates should be monitored for at least 24 hours [11]. Early feeding, ideally with breast milk, is advised. In severe situations, glucagon may be delivered (1 mg in children ≥ 12 years or ≥ 25 kg; 0.5 mg in younger children), while intravenous dextrose should be given as a bolus of 200-500 mg/kg (2-5 mL/kg of 10% dextrose) followed by continuous infusion to maintain euglycemia [12]. The first-line therapy for hyperinsulinemic hypoglycaemia is diazoxide it decreases insulin secretion by opening pancreatic -cell K_{ATP} channels. It is administered in divided dosages of 5-15 mg/kg/day, usually with a thiazide diuretic to minimize fluid retention. For diazoxide-unresponsive instances, octreotide (5-20 μ g/kg/day) can be utilized to suppress insulin release.

In acute circumstances, glucagon infusion can act as a brief supplement to reduce glucose requirements.[7]

Aims and Objectives

Primary Objective

- To study the clinical and biochemical profile of pediatric hypoglycemia.

Secondary Objectives

- To identify etiological distribution
- To correlate biochemical patterns with final diagnosis

METHODOLOGY

This observational case series was conducted at a tertiary care teaching hospital ,Osmania General Hodspital .Children aged 1 month to 12 years with plasma glucose ≤50 mg/dL and complete clinical and biochemical records were included. Cases with incomplete data were excluded. Data on demographics, clinical features, anthropometry, laboratory parameters during hypoglycemia, final diagnosis, and treatment were extracted from records. Continuous variables are presented as mean ± SD, and categorical variables as frequency and percentage.

RESULTS

A total of **20 children** with documented hypoglycemia were included in this case series. There were **12 males (60%) and 8 females (40%)**, with ages ranging from the neonatal period to 7.2 years. Consanguinity was present in a subset of cases, predominantly among those with metabolic and hyperinsulinemic etiologies.

Table 1:Demographic and Clinical Characteristics

CASE NO	GENDER	AGE	CONSANGUINITY	CLINICAL PRESENTATION
1	M	4 years	no	loss of conciousness
2	M	2.3years	no	fasting hypoglycemia
3	F	7.2 years	no	fasting hypoglycemia
4	M	5months	yes	loss of conciousness
5	M	21 day old	yes	fasting hypoglycemia
6	M	9month	no	loss of conciousness
7	M	4year	yes	seizures
8	M	5years	no	recurrent hypoglycemia
9	F	3years	yes	seizures
10	M	15month	no	fasting hypoglycemia
11	M	2years	yes	seizures
12	M	2 year 6month	no	seizures
13	F	2yr 10 month	no	seizures
14	M	2years	no	seizures
15	M	5year3months	yes	seizures
16	F	45 day old	no	fasting hypoglycemia
17	F	5year	no	fasting hypoglycemia
18	F	2yr 3 months	no	fasting hypoglycemia
19	F	3 years	yes	loss of conciousness
20	F	5 years	no	loss of conciousness

The most common presenting features were **fasting hypoglycemia, seizures, and altered sensorium/loss of consciousness**..Younger infants were more likely to present with neuroglycopenic symptoms, whereas older children often presented with fasting-related hypoglycemia.

Anthropometric Profile

Children with ketotic hypoglycemia generally had normal or mildly reduced growth parameters. In contrast, those with endocrine and metabolic disorders demonstrated **lower height and weight SDS**. Growth failure was particularly evident in children with growth hormone deficiency and glycogen storage disorders.

Table 2:Anthropometric Parameters

CASE NO	GENDER	AGE	HEIG HT	WEIGHT	HT SDS	WEIG HT SDS
1	M	4 years	94.1cm	11.5kg	-2	-2
2	M	2.3years	82.1cm	11.5KG	-4	-2
3	F	7.2 years	121 cm	34 kg	0	1.88
4	M	5months	52cm	7 kg	0	0
5	M	21 day old	50 cm	1.74 kg	0	0
6	M	9month	56cm	12.4kg	0	0
7	M	4year	101cm	12kg	-3.4	-2
8	M	5years	121cm	16kg	-3.4	-2
9	F	3years	94cm	12kg	-2	0.67
10	M	15month	49cm	11kg	-2	-2
11	M	2years	68cm	10kg	-0.6	0
12	M	2 year , 6m	75cm	11.7kg	-1.2 8	-1.28
13	F	2yr 10 month	78cm	10kg	-1.2 8	-2.1
14	M	2years	73cm	16.6kg	0.67	-1.28
15	M	5 year 3 months	106cm	17kg	-3.4	-2
16	F	45 day old	54cm	4kg	-0.4	0
17	F	5year	86cm	12kg	-0.6	0.67
18	F	2yr 3 months	84cm	5kg	-2.4	-2.4
19	F	3 years	77cm	8.5kg	-3.2	-2.1
20	F	5 years	112cm	12kg	-3.3	-2.1

Table 3:Biochemical Parameters During Hypoglycemia

CASE NO	GLU COSE (mg/dl)	INSU LIN (MiU /L)	C- PEPTIDE (ng/ml)	KET ONE	LACTAT E	GH (ng/ ml)	COR TISO L (mcg /dl)
1	32	1.6	0.5	5.8	N	18	28.3
2	41	4.6	0.8	0.02	N	3.18	31.8
3	49	20.3	0.9	0.01	N	16	29.8
4	39	7.9	0.8	0.3	N	15	48.8
5	35	10	1	0.1	N	16	8.4
6	34	29	1.2	0.12	N	14	4.7
7	33	6	1.9	0.14	N	1.29	8.8
8	36	2	0.5	6.1	N	0.41	8.3
9	37	9	1.6	0.2	N	14	11.9
10	34	1.4	1.4	0.2	N	14	13
11	40	6.14	1.8	0.18	N	12	15
12	42	0.5	0.2	0.04	elevated	0.21	76
13	35	0.7	0.3	0.02	elevated	12	32
14	36	0.1	0.86	0.05	N	10	23
15	34	0.2	0.4	5.8	N	4.43	54
16	36	0.5	1.86	0.12	N	12	51
17	38	5.3	0.4	0.02	N	18	27.5
18	40	9.8	1.91	0.17	N	18	27
19	34	0.3	0.3	0.18	elevated	14	26
20	34	0.1	0.14	0.58	N	3	13

The average plasma glucose concentration at presentation was 36.9 mg/dL. Different biochemical trends were found across etiological groupings. Children with hyperinsulinemic hypoglycemia exhibited improperly detectable insulin and C-peptide levels during hypoglycemia, as well as reduced ketone levels. The mean insulin and C-peptide levels were higher than the plasma glucose values. Children with ketotic hypoglycemia and hormonal deficits have high ketone levels along with adequately suppressed insulin levels. Counter-regulatory hormone testing indicated low or abnormally normal growth hormone and/or cortisol levels in children with endocrine abnormalities. Elevated lactate and ammonia levels were seen in children with metabolic problems, which helped with etiological classification.

Etiological Distribution

The most common etiology was **hyperinsulinemic hypoglycemia**, accounting for **12 cases (60%)**. Metabolic disorders, including **glycogen storage disease and gluconeogenic defects**, were identified in **4 cases (20%)**. **Idiopathic ketotic hypoglycemia** was diagnosed in **2 children (10%)**, while **growth hormone deficiency** accounted for **2 cases (10%)**.

Management and Outcome

Children with hyperinsulinemic hypoglycemia were treated with **diazoxide**, with or without hydrochlorothiazide, and showed clinical improvement with reduced hypoglycemic episodes. Children with ketotic hypoglycemia responded well to dietary modifications, including frequent feeds and avoidance of prolonged fasting. Hormonal deficiencies were managed with hormone replacement therapy, while metabolic disorders required disease-specific dietary and medical interventions.

Table 4: Etiological Distribution, treatment

CASE NO	DIAGNOSIS	MUTATION	TREATMENT
1	idiopathic ketotic hypoglycemia		small frequent feeds
2	hyperinsulinemic hypoglycemia		diazoxide
3	hyperinsulinemic hypoglycemia		diazoxide
4	hyperinsulinemic hypoglycemia		diazoxide
5	hyperinsulinemic hypoglycemia		diazoxide ,hydrochlorthiazide
6	hyperinsulinemic hypoglycemia	KCNJ11	diazoxide , inj . Octreotide
7	hyperinsulinemic hypoglycemia	ABCC8	diazoxide
8	growth hormone deficiency		Growth hormone therapy
9	hyperinsulinemic hypoglycemia	ABCC8	diazoxide
10	hyperinsulinemic hypoglycemia	KCNJ11	diazoxide, octreotide
11	hyperinsulinemic hypoglycemia	KCNJ11	diazoxide, hydrochlorthiazide
12	glycogen storage disease		small frequent feeds
13	glycogen storage disease		small frequent feeds
14	hyperinsulinemic hypoglycemia	ABCC8	diazoxide

15	idiopathic ketotic hypoglycemia		small frequent feeds
16	hyperinsulinemic hypoglycemia	ABCC8	diazoxide
17	gluconeogenic defect		small frequent feeds
18	hyperinsulinemic hypoglycemia	KCNJ11	inj. Octreotide , diazoxide
19	glycogen storage disease		small frequent feeds
20	growth hormone deficiency		Growth hormone therapy

DISCUSSION

This case series focuses on the clinical and biochemical range of pediatric hypoglycemia in a tertiary care context, as well as the diagnostic problems posed by age-related etiological heterogeneity. A organized diagnostic approach, including critical sample analysis, is required for correct etiological classification. The most common cause was hyperinsulinemic hypoglycemia (HI), which was defined by low ketone levels, detectable insulin and C-peptide during hypoglycemia, and increased glucose infusion requirements. Early detection of Hyperinsulinemic hypoglycemia is critical to avoiding recurring severe hypoglycemia and negative neurodevelopmental effects. Endocrine reasons, particularly growth hormone and cortisol deficit, accounted for a subgroup of cases and were characterized by ketotic hypoglycemia and insufficient counter-regulatory hormonal responses. Inborn metabolic mistakes, including as glycogen storage and fatty acid oxidation disorders, were less common but showed up early with recurring episodes and other biochemical abnormalities such increased lactate or ammonia. The most common presenting signs were seizures and impaired sensorium, indicating that hypoglycemia was not recognized early enough. Children with endocrine and metabolic diseases exhibited lower growth metrics, emphasizing the diagnostic value of anthropometry. Distinct biochemical trends across etiologies highlight the importance of extensive critical sampling in the assessment of pediatric hypoglycemia.

CONCLUSION

Pediatric hypoglycemia requires a structured diagnostic approach. Etiology-based interpretation of biochemical parameters improves diagnostic accuracy and outcomes. This study emphasizes that early etiological classification of hypoglycemia allows targeted therapy, such as diazoxide for hyperinsulinemic hypoglycemia or hormonal replacement in endocrine deficiencies, thereby preventing recurrent episodes and long-term neurological sequelae. Incorporating standardized hypoglycemia evaluation protocols in emergency and pediatric settings may improve outcomes.

LIMITATIONS

Small sample size, Lack of long-term neurodevelopmental follow-up

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