

GUIDELINE FOR EVALUATION AND MANAGEMENT OF NEONATAL HYPOGLYCAEMIA



Ministry of Health

Male' Republic of Maldives

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Introduction

Hypoglycemia is a common phenomenon in neonates. Transient low blood glucose levels in neonates are common as the source of glucose at delivery changes from a continuous supply from the mother to the intermittent supply from feeds.

However, there is no single consistent definition for this condition because the normal range of blood glucose is variable and depends upon many factors.

It has been difficult to establish a single numerical blood glucose level that accurately predicts significant neonatal hypoglycemia at which intervention should be initiated to prevent morbidity. As a result, operational thresholds have been proposed to provide a margin of safety. The operational threshold for hypoglycemia is defined as that blood glucose level at which clinicians should consider intervention.

With loss of the continuous transplacental infusion of glucose, plasma glucose concentration in the healthy term newborn falls during the first two hours after delivery, reaching a nadir in 1- 2 hours of life, these levels are transient and begin to rise and stabilizes by four to six hours of age. This observation is considered to be part of the normal adaptation for postnatal life that helps establish postnatal glucose homeostasis. Since hypoglycemia is a common phenomenon, proper guideline is needed to systematically address and manage the condition to prevent possible complications and effects of hypoglycemia.

This guideline is intended for the evaluation and management of infants under 28 days of life with Hypoglycemia in Maldives.

Case definition

For Practical operational threshold, Hypoglycemia is defined as blood glucose level of less than 45 mg/dL.

Screening for hypoglycemia

Blood glucose concentration **should be measured** in

1. infants at risk for hypoglycemia
2. in infants who exhibit signs or symptoms consistent with hypoglycemia.

Indication for routine blood glucose screening:

1. Preterm infants (≤ 35 weeks)
2. Low birth weight infants (< 2000 gm)
3. Small for gestational age infants (SGA): birth weight < 10 th percentile
4. Large for gestational age (LGA) infants: birth weight > 90 th percentile
5. Infants with Rh-hemolytic disease
6. Infants with IUGR.
7. Any sick neonate (e.g., perinatal asphyxia, polycythemia, sepsis, shock etc), during sickness. Once their condition gets stabilized, screening may be discontinued
8. Infants on Total parenteral nutrition
9. Infants born to mother on oral hypoglycemic drugs, beta blockers.

Time schedule of blood glucose monitoring

1. At risk neonates (e.g., preterm, L.B.W, S.G.A, L.G.A), Infant of diabetic mother: 2, 6, 12, 24, 36, 48 hours.
2. Sick infants (Infants with sepsis, asphyxia, shock)during active phase of illness: Every 6-8 hours (individualize as necessary)

Method of blood glucose level estimation

Use Glucometer with test strips

Place: side of Heel of foot (see picture: darkened area), do not squeeze.

Never take Blood glucose level from a venous or arterial line where Glucose is infusing.

Test-strip results demonstrate a reasonable correlation with actual plasma glucose concentrations, but the variation from the actual level may be as much as 10 to 20 mg/dl.

Thus, hypoglycemia determined by a glucometer should be confirmed by laboratory measurement. Initiate appropriate treatment immediately before confirmatory results are available.

Prompt laboratory analysis should be performed because a delay between blood sample collection and laboratory analysis may produce a falsely low Blood glucose level reading.



Clinical signs and symptoms

The clinical signs and symptoms of neonatal hypoglycemia are not specific and include a wide range of local or generalized manifestations that are common in sick neonates.

- Jitteriness, tremors, irritability,
- Seizures,
- Cyanosis,
- Apneic episodes, tachypnea
- Weak and high-pitched cry,
- Floppiness or lethargy, coma

- Sweating, sudden pallor, tachycardia
- Temperature instability
- Poor feeding
- Eye-rolling.

Because these are nonspecific signs and symptoms, further evaluation for other possible causes (eg, sepsis) should be conducted if symptoms do not resolve after normalization of the blood glucose concentration.

Preventative care

Keep baby warm.

Maintain normothermic temperature.

Early skin-to-skin contact if baby's gestation and condition permitting.

Initiate early feeds within 30-60 minutes of birth then 2- 3 hourly.

Avoid separation of mother and baby.

Management of Hypoglycemia

1. Infants with asymptomatic hypoglycemia

Asymptomatic hypoglycemia is said to be present when blood glucose level is < 45 mg/dL and the infant does not manifest any clinical features.

✓ Blood sugar 20 - 45 mg/dL (asymptomatic)

- Give trial of oral feeds (breast feeding, expressed breast milk or formula) and check blood glucose after 1 hour.
- If repeat Blood glucose level is >45 mg/dL, feed two hourly with 6 hourly monitoring of Blood glucose for 48 hrs.

The target blood glucose value is 50 to 120 mg/dL.

- If repeat blood sugar is < 45 mg/dL, start I.V dextrose and for further management follow algorithm.
- Maintain a normothermic environment

✓ **Blood sugar levels <20 mg/dL**

- Management is similar as symptomatic hypoglycemia.
- Give Bolus of 2 mL/kg of 10% dextrose (200 mg/kg) over one minute.
- Start IV Dextrose with Glucose Infusion rate (GIR) of 6 mg/kg/min of glucose after bolus and for further management follow algorithm.

$$\text{Glucose Infusion Rate (GIR)} = \frac{\text{I.V fluid rate (mL/kg/day)} \times \% \text{ of dextrose}}{144}$$

e.g Newborn receiving 80ml/kg /day of 10 % dextrose

$$\text{GIR} = 80 \times 10 \div 144$$

$$\text{GIR} = 5.5 \text{ mg/kg/min}$$

2. Management of symptomatic hypoglycemia

Symptomatic hypoglycemia is said to be present if hypoglycemia (Blood glucose <45 mg/dL) presents with clinical symptoms.

- Give Bolus of 2 mL/kg of 10% dextrose (200 mg/kg) over one minute.
- The bolus should be followed by continuous glucose infusion at an initial rate of 6 mg/kg/min.

After bolus, continuous glucose infusion is needed, otherwise it will cause rebound hypoglycemia.

Monitoring and Further management during treatment for hypoglycemia

- Check Blood glucose every 30 to 60 min until blood sugar is >50 mg/dl and then every 6 hour.
- If Blood glucose is still <45 mg/dL despite bolus and glucose infusion, increase glucose infusion rate (GIR) by 2 mg/kg/min every 30 min until a maximum of 12 mg/kg/min.
 - Use increased volume with caution in infants where volume overload is a concern. If risk of fluid overload, increase concentration rather than volume. Maximum fluid is 100 mL/kg/day on day 1 of life. Monitor serum sodium levels as patient may develop dilutional hyponatraemia.
- Increase dextrose concentration in increments of 2.5% (e.g., 12.5% ,15%, 17.5 %, maximum up to 20 %).
- Do not use $> 12.5\%$ dextrose infusion through a peripheral vein due to the risk of thrombophlebitis.
 - If infant requires IV dextrose concentrations $>12.5\%$, insert central venous catheter.
- If Blood glucose is <45 mg/dL despite glucose infusion rate (GIR) of 12 mg/kg/min., send blood sample for determination of the cause for persistent hypoglycemia then give Hydrocortisone 5 mg/kg/day IV in two divided doses for 24 to 48 hrs.
- After 24 hours of IV glucose therapy, if two or more consecutive Blood glucose level are >50 mg/dL, then infusion can be tapered off at the rate of 2 mg/kg/min every 6 hourly with Blood glucose monitoring.

Tapering has to be accompanied by simultaneous increase in oral feeds.
- Once a rate of 4 mg/kg/min of glucose infusion is achieved and oral intake is adequate and the Blood glucose level are consistently >50 mg/dL, infusion can be stopped.
- Do not stop glucose infusion abruptly as severe rebound hypoglycemia may occur.

Indications for I.V therapy in Neonatal hypoglycemia

- Inability to tolerate oral feeding.
- Symptomatic.
- Not maintaining normal glucose level despite oral feeds.
- Blood glucose level < 20 mg/dL.

Recurrent / persistent hypoglycemia

When infant fails to maintain normal Blood glucose level despite a GIR of 12 mg/kg/min or early onset hypoglycemia that is persisting/recurring after 72 hours. Further evaluation should be done to find the cause.

First ensure I.V line is patent and check concentration of the IV fluid and rate.

Causes of Recurrent/persistent Neonatal hypoglycemia:

- Endocrine deficiency
 - Hypopituitarism
 - Growth hormone deficiency
 - Glucagon deficiency
 - Cortisol deficiency
- Hyperinsulinism
- Glycogen storage disease
- Disorders of carbohydrate metabolism, amino acid metabolism, fatty acid metabolism

When blood glucose level is < 50 mg/dL, send blood sample for (as per availability)

- blood glucose
- insulin, C-peptide
- Free fatty acids

- Cortisol
- Growth hormone,
- Thyroid function test
- Blood gas analysis
- Plasma amino acids
- Ammonia, pyruvate
- Urinary ketone
- collect next passed urine for Urinary metabolic profile

Drugs for Hypoglycemia

For persistent, recurrent hypoglycemia:

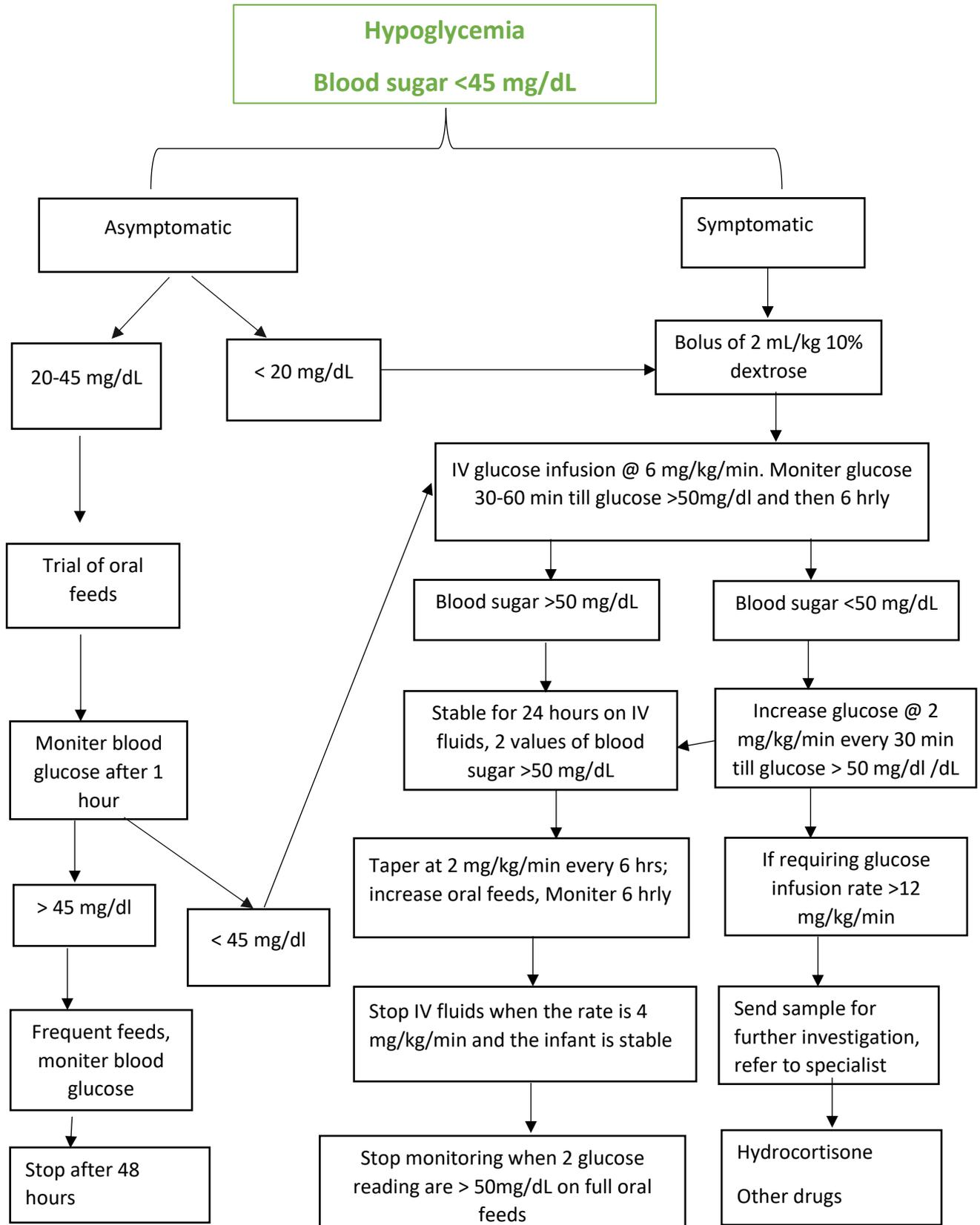
- Hydrocortisone: 5 mg/kg/day IV or PO in two divided dose for 24 to 48 hrs.
- Diazoxide: orally 10-25 mg/kg/day in three divided dose (used in hyperinsulinism, insulinomas)
- Glucagon: 100 µg/kg subcutaneous or intramuscular (max 300 µg) – maximum of 3 doses.
- Octreotide: 2-10 µg/kg/day subcutaneously two to three times a day.

Follow-up and outcome

There is not a specific plasma glucose concentration or duration of hypoglycemia that can predict permanent neurologic injury.

Severe (eg., associated with seizures or altered level of consciousness), persistent or recurrent hypoglycemia should be followed up at 1, 3, 6, 9, 12 and 18 months corrected age for monitoring vision, hearing, growth and neurodevelopment.

Neonatal Hypoglycemia: Algorithm



How to prepare required Intravenous Fluid Concentration

5 % dextrose (Total: 50 ml)	10 % dextrose - 25 ml
	Distilled water - 25 ml
7.5 % dextrose (Total: 50 ml)	10 % dextrose - 38 ml
	Distilled water - 12 ml
12.5 % dextrose (Total: 50 ml)	10 % dextrose - 40 ml
	25 % dextrose - 9 ml
	Distilled water - 1 ml
15 % dextrose (Total: 50 ml)	10 % dextrose - 30 ml
	25 % dextrose - 18 ml
	Distilled water - 2 ml
17.5 % dextrose (Total: 50 ml)	10 % dextrose - 10 ml
	25 % dextrose - 31 ml
	Distilled water - 9 ml
20% dextrose (Total: 50 ml)	25 % dextrose - 40 ml
	Distilled water - 10 ml
N/5 5% dextrose (Total: 50 ml)	10 % dextrose - 25ml
	Distilled water - 15 ml
	Normal saline - 10 ml
N/5 7.5% dextrose (Total: 50 ml)	10% dextrose - 39 ml
	Distilled water - 1 ml
	Normal saline - 10 ml
N/5 10% dextrose (Total: 50 ml)	10 % dextrose - 25 ml
	25% dextrose - 10 ml
	Distilled water - 5ml
	Normal saline - 10 ml
N/5 12.5 % dextrose (Total: 50 ml)	10 % dextrose - 25 ml
	25 % dextrose - 15 ml
	Normal saline - 10 ml
N/5 15 % dextrose (Total: 50 ml)	10% dextrose - 15 ml
	25% dextrose - 24 ml
	Distilled water - 1ml

	Normal saline - 10 ml
N/5 17.5 % dextrose (Total: 50 ml)	10% dextrose - 7 ml
	25 % dextrose - 32 ml
	Distilled water - 1ml
	Normal saline - 10 ml
N/5 20% dextrose (Total: 50 ml)	25 % dextrose - 39 ml
	Distilled water - 1ml
	Normal saline - 10 ml

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