NEONATAL HYPOGLYCAEMIA

Definition:

Operational threshold is defined as a plasma or whole blood glucose concentration at which clinicians should consider intervention. A blood glucose level (BGL) of less than 40 mg/ dl (plasma glucose <45 mg/dl) has been taken as the operation threshold for intervention. The WHO defines hypoglycaemia as a BGL of less than 45 mg/dl (2.2 mmol/L.)

Blood glucose levels as low as 30 mg/dl within 1-2 hours of birth are common in normal newborns. The term "transitional neonatal hypoglycaemia" (TH) has been used to describe this transient phenomenon. TNH occurs in up to 10% of normal newborns and represents a normal physiological adaptation to postnatal life.

The American Academy of Paediatrics (AAP) has provided guidelines for screening at-risk newborns and an algorithmic approach to management if the plasma glucose is lower than 40 mg/dl in the first 24 hours.

Indication for routine screening

- Birth weight <2kg
- Gestational age ≤35 weeks
- Small for gestational age infants (SGA)
- Infant of diabetic mothers (IDM)
- Large for gestational age (LGA) infants
- Neonates born to mothers receiving therapy with
    - terbutaline/propranolol/labetalol/oral hypoglycaemic agents.
- Any sick neonate, e.g. those with perinatal asphyxia, polycythaemia, sepsis shock, etc. during the acute phase of illness
- Family history of a genetic form of hypoglycaemia
- Congenital syndromes (e.g. Beckwith-Wiedernann), abnormal physical features (e.g. midline facial malformations, microphallus
- On parenteral nutrition.

Schedule of blood glucose monitoring

Category of infants	Time schedule
At-risk neonates	**2,6,12,24,48 and 72 hours of life**
Sick neonates *	**Every 6-8 hours**
Neonates on parenteral nutrition-	• **Initial 72 hours: every 6-8 hours** • **After 72 hours: once a day**

*sepsis, asphyxia, polycythaemia, shock during acute phase of illness

SYMPTOMS OF HYPOGLYCEMIA

- Usually asymptomatic.
- **Neurogenic (autonomic)** - sympathetic nervous discharge -include both adrenergic and cholinergic responses.
- **Neuroglycopenic symptoms** -deficient supply of primary fuel (glucose) to the brain - **stupor, jitteriness tremors, apathy, episodes of cyanosis, convulsions, intermittent apneic spells or tachypnoea, weak and high-pitched cry, lethargy, and difficulty in feeding**. ***Episodes of sweating, sudden pallor, hypothermia, cardiac arrest*** have also been reported.

DIAGNOSIS

Asymptomatic hypoglycaemia is said to be present when BGL is less than 40 mg/dl (to be confirmed by laboratory estimation), but the infant does not manifest any clinical features.

Symptomatic hypoglycaemia should be diagnosed if hypoglycaemia (BGL is <40 mg/dl) coexists with clinical symptoms.

- Neonates generally manifest nonspecific signs that result from a variety of illnesses. Therefore, careful evaluation should be done to look for all possible causes, especially those attributed to hypoglycaemia.
- If clinical signs attributable to hypoglycaemia persist despite intravenous glucose, then other causes of persistent/resistant hypoglycaemia should be explored.

Indication of admission

- TO WARD: Asymptomatic hypoglycaemia (BGL <40mg/dl) whose post feed BGL are >50mg/dl
- TO NICU:
    - Any case of symptomatic hypoglycaemia
    - Asymptomatic hypoglycaemia if 1st reading is < 20mg/dl
    - Asymptomatic hypoglycaemia if 2 consecutive BGL readings are <40mg/dl measured post feed and after correcting hypothermia.

Management of Asymptomatic Hypoglycaemia

- Direct breastfeeding is the best option for a trial of oral feeding. If the infant cannot suck, expressed breast milk may be given. Breast milk promotes ketogenesis (ketones are important alternative sources for the brain, along with other sources such as pyruvate, free fatty acids, glycerol, and amino acids).
- If breast milk is not available, then formula feeds may be given.

Management of Symptomatic Hypoglycaemia

- All symptomatic infants should be treated with IV fluids. A 2 mg/kg of bolus of 10% dextrose (200 mg/kg) should be given for symptomatic hypoglycaemia (including seizures).
- The bolus should be followed be continuous glucose infusion at 6-8 mg/kg/min. Blood sugar should be checked after 30 min and then every 6 hours until blood sugar is >50 mg/dl.
- If BGL stays below 50 mg/ dl despite bolus and glucose infusion, glucose infusion rate (GIR) should be increased in steps of 2 mg/kg/min every 15-30 min until a maximum of 12 mg/kg/min.

- **After 24 hours of IV glucose therapy, once two or more consecutive BGLs are >50 mg/dl, the infusion can be tapered off at 2 mg/kg/ min every 6 hours with BGL monitoring. A concomitant increase in oral feeds must accompany tapering.**
- **Once a rate of 4 mg/kg/min of glucose infusion and adequate oral intake is achieved, and the BGLs are consistently above 50 mg/dl, the infusion can be stopped.**

It is vital to ensure continuous glucose infusion, preferably using an infusion pump without interruption. Do not stop glucose infusion abruptly, as severe rebound hypoglycaemia may occur.

Avoid using more than 12.5% dextrose infusion through a peripheral vein due to the risk of thrombophlebitis.

Practical tip: If there is persistent hypoglycaemia, check the intravenous line for patency. Also, recheck the intravenous fluid preparation and infusion rate.

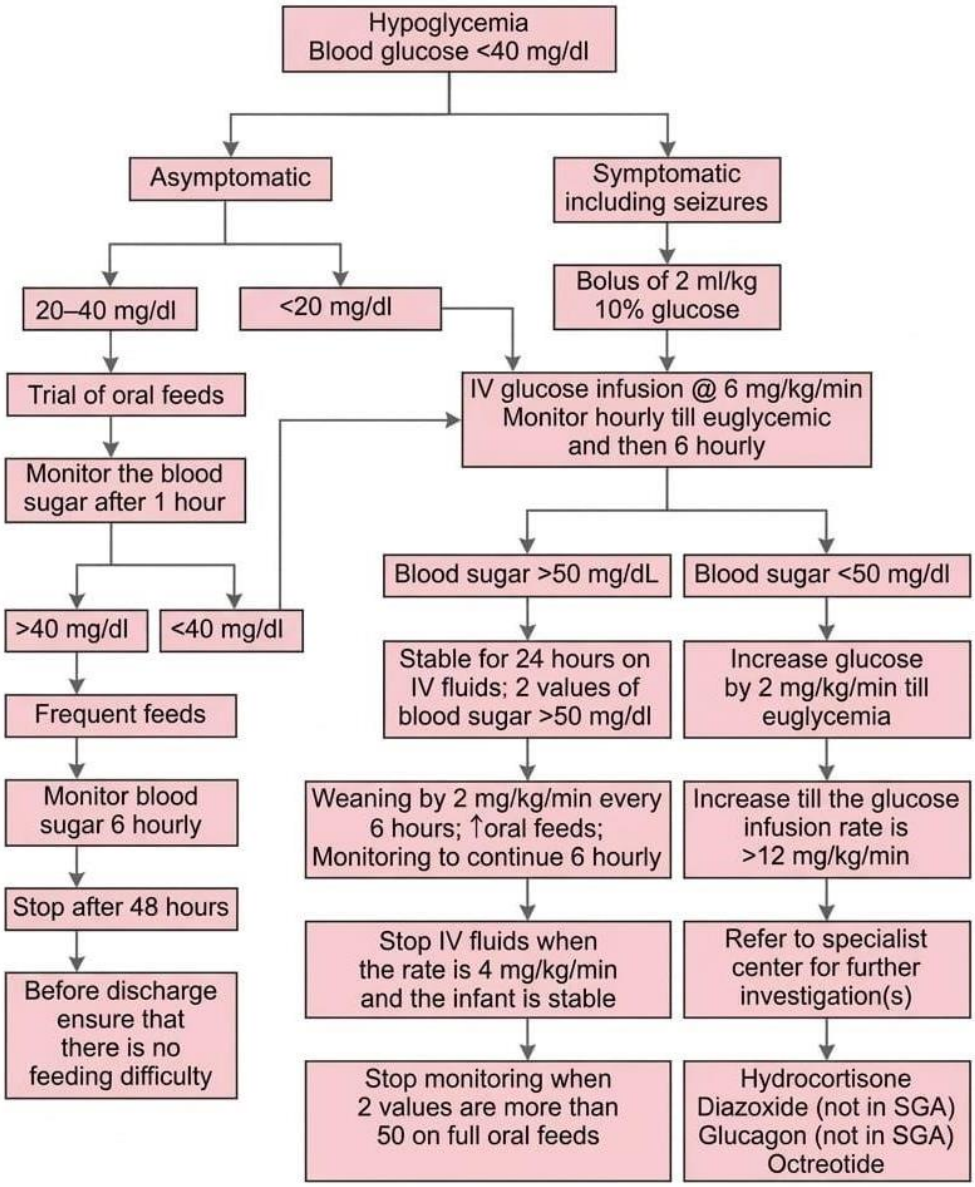

Fig. 28.1: Algorithm for management of neonatal hypoglycemia

Recurrent/resistant Hypoglycaemia

When the infant fails to maintain normal **BGL despite a GIR of 12 mg/kg/min or when stabilization is not achieved by 7 days of therapy.**

Hyperinsulinism must be excluded because it is the most common cause of persistent hypoglycaemia.

Criteria for diagnosis of hyperinsulinism:

Critical sample must be drawn at time of hypoglycaemia (blood glucose<40)

1. **Detectable insulin (>2 m/U/L); usual levels with hyperinsulinism are >5-10**
2. **Low free fatty acids (<1.5 mmol/L).**
3. **Low ketones (plasmaß hydroxybutyrate <2.0 mmol/L).**

4.Inappropriate glycaemic response to 0.1 mg/kg intravenous glucagon at the time of hypoglycaemia normally glucose rise >30 mg/dl in 20 minutes.

Table 28.5: Investigations to be done in resistant hypoglycemia*

Blood	*Urine*
• Serum insulin levels, C-peptide, IGFBP3, thyroid hormones • Serum cortisol levels • Growth hormone levels Serum ammonia • Serum lactate levels, free fatty acids, blood BOHB Galactose 1 phosphate uridyl transferase levels • Tandem Mass spectroscopy (TMS) Genetic testing for mutations like SUR1 and KiR6.[2]	• Urine ketones • Urine reducing substances • Urine GCMS

Table 28.6: Treatment options in resistant hypoglycemia				
Drug	*Dose*	*Route*	*Mode of action*	*Side effects*
Hydrocortisone	10 mg/kg/ day BD	PO /IV	Reduces peripheral glucose utilization Increases gluconeogenesis Increases glucagon effect	Hyperglycemia, hypertension
*Diazoxide**	5–15 mg/ kg/day TDS	PO	K channel agonist	Fluid retention, *hypertrichosis, cardiac failure*
Octreotide	5–35 mcg/ kg/day TDS/QID	S/C	Somatostatin analogue inhibits insulin secretion	Cholelithiasis, transient growth impairment, tachyphylaxis
*Glucagon**	0.2 mg/kg	S/C or IM	Glycogenolysis, increased gluconeogenesis	Nausea, vomiting, skin rash, rebound hypoglycemia

FOLLOW-UP

- **At 3, 6,9, 12, and 18 months of corrected age**, they need to be followed up for **growth, neurodevelopment, vision, and hearing loss.** Vision can be assessed with the Teller acuity cards while hearing is assessed by brainstem-evoked auditory responses.
- **MRI at 4-6 weeks** provides a good estimate of hypoglycemic injury and should be considered in the follow-up of such infants.

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Guideline accepted date	**January 2025**
Guideline review date	**January 2027**