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SCREENING, IDENTIFYING AND MANAGING INFANTS AT-RISK OF HYPOGLYCAEMIA TO PREVENT NEURONAL INJURY

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Background: Hypoglycemia during the neonatal period can cause ***severe brain injury***. Although hypoglycemia in term neonates is usually "transitional", prolonged or persistent (Genetic) hyperinsulinemic hypoglycemia (HH) may occur in those **"at-risk"** of hypoglycemia.

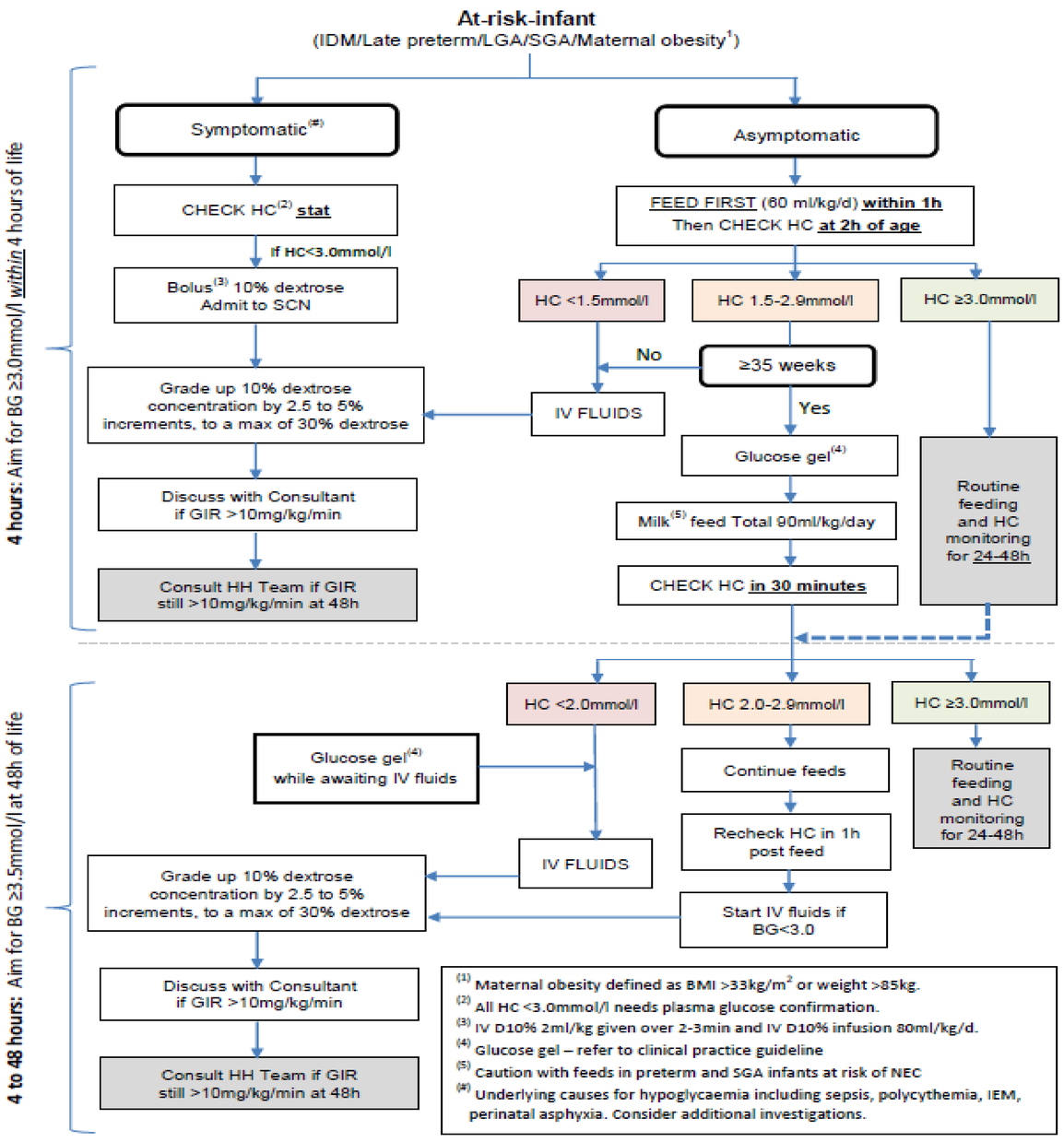
Physiological basis: In term neonates, foetal to neonatal glucose transition stabilizes within 48h of life, whereas transition may take longer in the at-risk group. At-risk infants discharged at 24h may encounter prolonged asymptomatic hypoglycemia in the home setting, putting them at risk of brain injury.

Gap: Infants at-risk of hypoglycemia comprise 25% of all pregnancies and include small for gestational age (SGA), large for gestational age (LGA), preterm and infants born to mothers who are obese and/or diabetic. The identification of these at-risk infants is a critical step that was previously ill-defined.

Objective: To streamline the screening, identification and treatment of these at-risk infants, we introduced a new evidence-based hypoglycemia screening pathway (Figure 1) and HH pathway (Figure 2) at our institution. We present the clinical features of infants identified with HH.

Definition of Hypoglycemia:
Blood glucose <3.0mmol/L before 48h of life
Blood glucose <3.5mmol/L after 48h of life

Figure 1: Hypoglycemia Algorithm For The At Risk Infant.



End Point 1: Full feeds established, normal BG after 48h, parents engaged
End Point 2: Meets criteria for HH – enter HH pathway

Methodology: Period of study: April – Dec 2015

Key steps: 1st hour of life: skin to skin and breast feeding, 1-2h: feed, care at the bedside, mother involved, mother-child bonding & breast feeding continues, glucose monitoring – supervision by trained nurses/doctors.

Hypoglycemia encountered: Allow metabolic transition. Encourage feeding. Use buccal Glucogel and extra feeds when hypoglycemic.

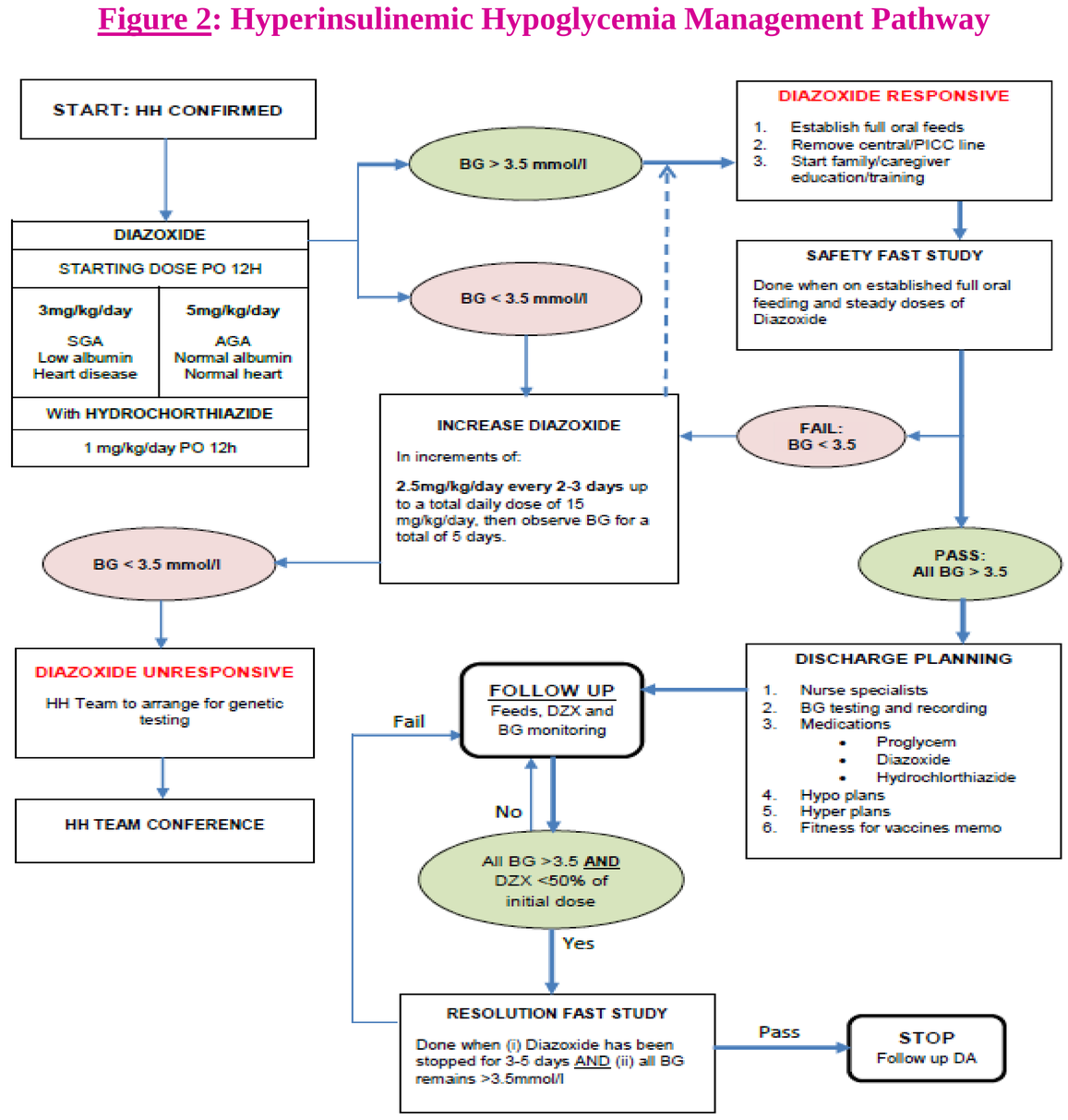
Still hypoglycemic: Slow IV glucose bolus and glucose infusion graded up to maintain normoglycemia. When glucose infusion rate (GIR) >10mg/ kg/min, initiate diagnostic work up for HH.

Characteristics of babies identified with HH:

- Institution Incidence: 2.3 per 1,000 (21/9175 live births)
- Birth weight: 2558g (1370-4725g)
- Gestational age: 36.8 weeks (34-40 weeks)
- Race: 11 Chinese, 6 Malay, 3 Indian, 1 Filipino

Diagnosis of Hyperinsulinemic hypoglycemia (HH):
GIR - >10mg/kg/min **after 48h of life**
Detectable insulin levels when BSL <3.0mmol/L
Hypoketonemia <0.6mmol/L, Hypofattyacidemia <0.5mmol/L

Figure 2: Hyperinsulinemic Hypoglycemia Management Pathway



End Point 3: Passes resolution fasting study
End Point 4: Diazoxide unresponsive – enter DZX unresponsive pathway

Results:

At-risk status: SGA: 14/21 babies (67%); LGA: 2/21 babies (none had GDM mothers); GDM: 3/21 babies (none were LGA); Prematurity: 9/21 babies (8 had multiple risk factors)

Clinical presentation and outcomes:

Onset of symptoms: Day 1 =18 and Day 2 =1 (during screening); Day 3=1 and Day 4=1 (discharged patients who were readmitted)

Signs: Jittery=3; Seizures=3. Babies with seizures were all male

Diazoxide (DZX) treatment: All were DZX responsive.

Genetic study done in 3 cases- 1 case of HNF4A mutation (MODY1) identified.

MRI: 2/3 symptomatic HH infants had MRI evidence of parieto-occipital injury.

Safety fast study: All of them passed safety fast study.

Resolution fast study was done in 14/21, who all passed and are off diazoxide.

Follow up: One SGA infant who had HH, has infantile spasm at 6 m of age.
Neurodevelopmental screening (Bayley III) to be done at 2 years.

Conclusions:

1. Incidence of HH in a population is being reported for the first time.
2. HH affects mostly preterm and term SGA infants, with a male preponderance.
3. 90% of the infants with HH present in the first 2 days of life.
4. All infants in this cohort with HH were Diazoxide responsive.
5. Genetic screening may be indicated in HH infants with strong family history of diabetes to rule out mutations in MODY genes (HNF4A, HNF1A and GCK gene).