Neonatal Hypoglycemia and Hyperinsulinaemia

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Introduction

- Neonatal hypoglycaemia is an important indicator of a number of underlying illness including inborn errors of metabolism and endocrine disorders.
- Hypoglycaemia does not always produce symptoms in newborn babies
- Clinical signs of neonatal hypoglycaemia are non-specific and are associated with other disorders common in neonate.
- Therefore presymptomatic monitoring at risk babies blood glucose levels will detect and prevent hypoglycaemic episodes. Severe hypoglycaemia to be further investigated.

Aims and Objectives

- To document the incidence and to record the cause and response to treatment of severe hypoglycaemia in otherwise well newborn babies born at Redland Hospital.

Material and Methods

- A retrospective case review of all babies admitted to our Specical Care Nursery from 2001 to 2006 for severe hypoglycemia was performed.
- Protocol for monitoring blood glucose in an otherwise well newborn baby was implemented at our hospital in 2001.
- Severe hypoglycaemia is defined as blood glucose less than 2mmol/l.
- Maternal and perinatal data was recorded.
- Preterm infants born <34 weeks gestation, Infants with perinatal asphyxia, external congenital anomaly and infection were excluded.

Material and Methods

- Redland hospital is an outer metropolitan district hospital covering a population of 190,000 in the Redland shire area of South-East Queensland
- Number of babies born increased from 1300 in 2001 to 1800 in 2006.
- Level 2 nursery with 6 bed capacity
- About 150 admissions per year

Material and Methods contd…

- **Maternal data included:**
- Age
- Parity
- Diabetic status (known or gestational), diet controlled/insulin treated
- Medication/complication/illness during pregnancy

- **Family history included**:
- Ethnicity of parents
- Affected siblings/family members

- **Neonatal data included**:
- Gestation
- Sex
- Birth weight/length/head
- Mode of delivery
- Birth trauma
- Apgar scores
- Timing of hypoglycemia
- Signs and symptoms
- Lowest BGE
- Number of hypoglycemic episodes
- Number of days on IV fluids
- Medications to treat hypoglycemia
- Surgical treatment
- Discharge examination

Protocol

- First blood glucose estimation (BGE) is performed prior to the second feed.
- First feed should be immediately after birth or within 2 hours of birth.
- First BGE should be a minimum of 2 hours after birth.
- Second BGE should be no later than 4 hours after first BGE.
- Once two consecutive BGE are $\geq$ 2.6mmol/ cease testing. This principle is excluded in the case of IUGR infants and infant of an insulin treated GDM mother.

Protocol contd…….

- IUGR infant and infant of insulin treated GDM must continue BGE at 6 hourly intervals for a following 24 hours
- If BGE are 2-2.6mmol/l continue testing 3-4 hourly before feeds until two consecutive BGE $\geq$ 2.6mmol/l. Baby continues to breast feed but a top-up is required, preferably EBM but formula may be used if EBM insufficient.
- If BGE less than 2.0mmol/l the pediatric registrar is notified

Protocol contd……

- If BGE less than 2.0mmol/l feed the baby at 80mls/kg/day by gavage feeds and repeat the BGE one hour post feed. If BGE remains less than 2.0mmol/l commence an IV at 80mls/kg per day 10% Dextrose.
- When an IV is commenced , blood should be taken for formal investigations of hypoglycemia.
- BGE should be performed 1hour after commencing or change in the rate that was initiated following a low BGE

Protocol contd……

- Initial blood sampling is from a capillary heel prick.
- BGE is performed by the designated ACCU-CHEK Advantage11 glucometer
- A formal venous blood sample is sent to the lab to confirm any BGE < 2 or repeated BGE <2.6mmol/l.

Blood glucose monitored on infants at risk of hypoglycemia in the following categories:

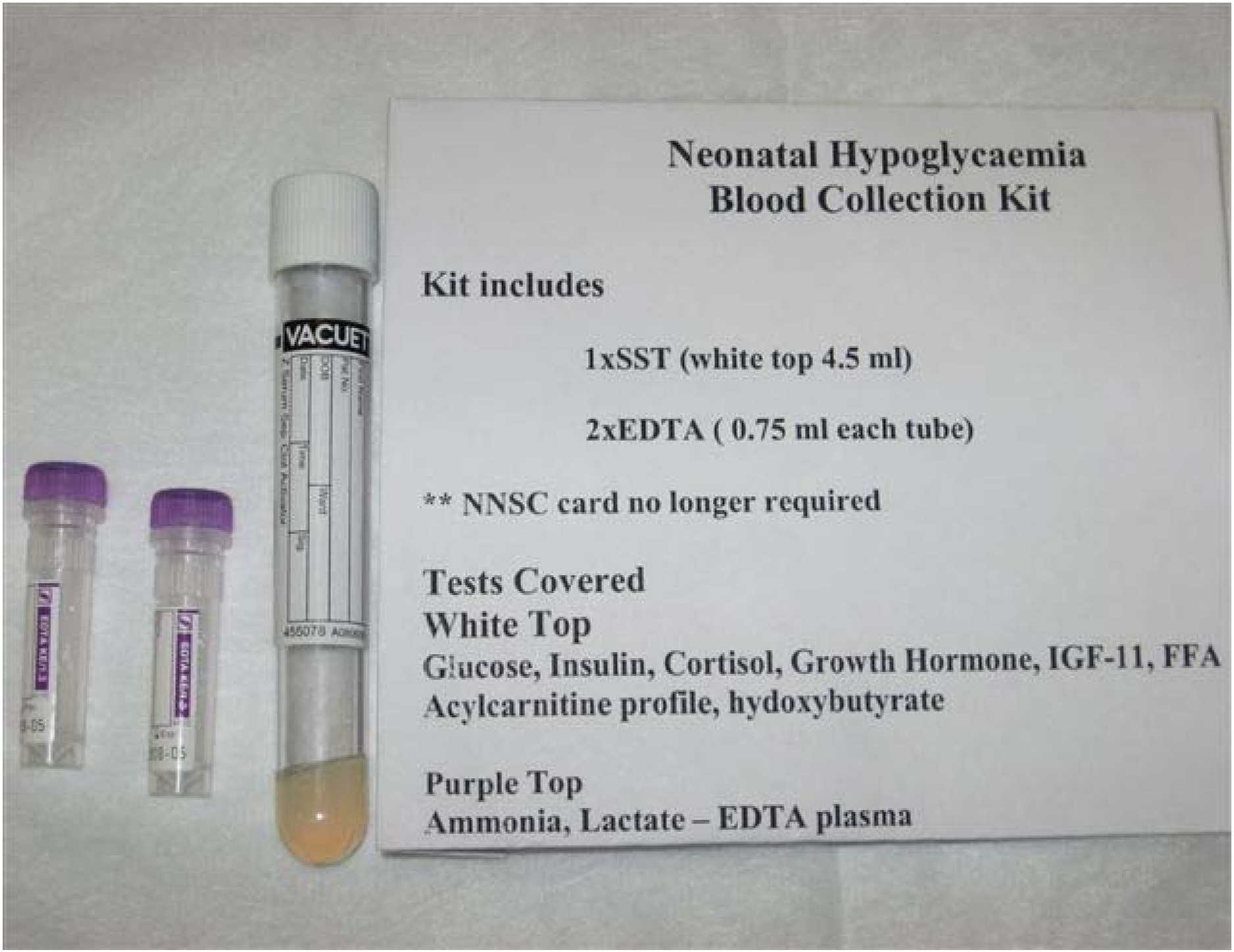
- Macrosomic infants greater than 97th percentile for weight or greater than 4.2kgs
- Low birth weight infants less than 2.5 kgs or less than 10th percentile
- Preterm infants less than 35 weeks gestation
- Scrawny, dysmature infants
- Infants of mothers who are diabetic or who have gestational diabetes
- Low 5 minute Apgar score (less than 7 at five minutes)
- Any newborn with symptoms suggestive of hypoglycemia- apnoea, seizures, tachypnoea, lethargy, poor suck or refusal to feed, temperature instability.

Neonatal Hypoglycaemia blood collection kit

- Kit includes: 1x SST (white top 4.5ml)
  2x EDTA (purple top 0.75ml each tube)

- Tests Covered
- White Top: Glucose, Insulin, GH, Cortisol, FFA, IGF-11, Acylcarnitine profile, hydroxybutyrate

- Purple Top: Ammonia, Lactate



Neonatal Hypoglycaemia Blood Collection Kit

Kit includes

1xSST (white top 4.5 ml)

2xEDTA (0.75 ml each tube)

** NNSC card no longer required

Tests Covered

White Top

Glucose, Insulin, Cortisol, Growth Hormone, IGF-11, FFA
Acylcarnitine profile, hydoxybutyrate

Purple Top

Ammonia, Lactate – EDTA plasma

Results

- 9498 Babies were born between 1st January 2001 and 31st December 2006 at Redland hospital.
- 663(6.98%) were large for gestational age (LGA)
- 145(1.52%) were small for gestational age (SGA) babies.
- Only 8 babies had severe hypoglycaemia.(< 2.0mmo/l)
- 6 of these babies were diagnosed as Hyperinsulinaemic based on inappropriately high insulin level and low ketones and fatty acids at the time of hypoglycaemia..
- 2 with Panhypopituitarism based on low serum Cortisol and Growth harmone levels at the time of hypoglycaemia.

Signs and Symptoms

- Asymptomatic (3)
- Poor feeding (2)
- Hypothermia (2)
- Respiratory distress (1)
- Apnoeic spell (1)
- Seizures (1)

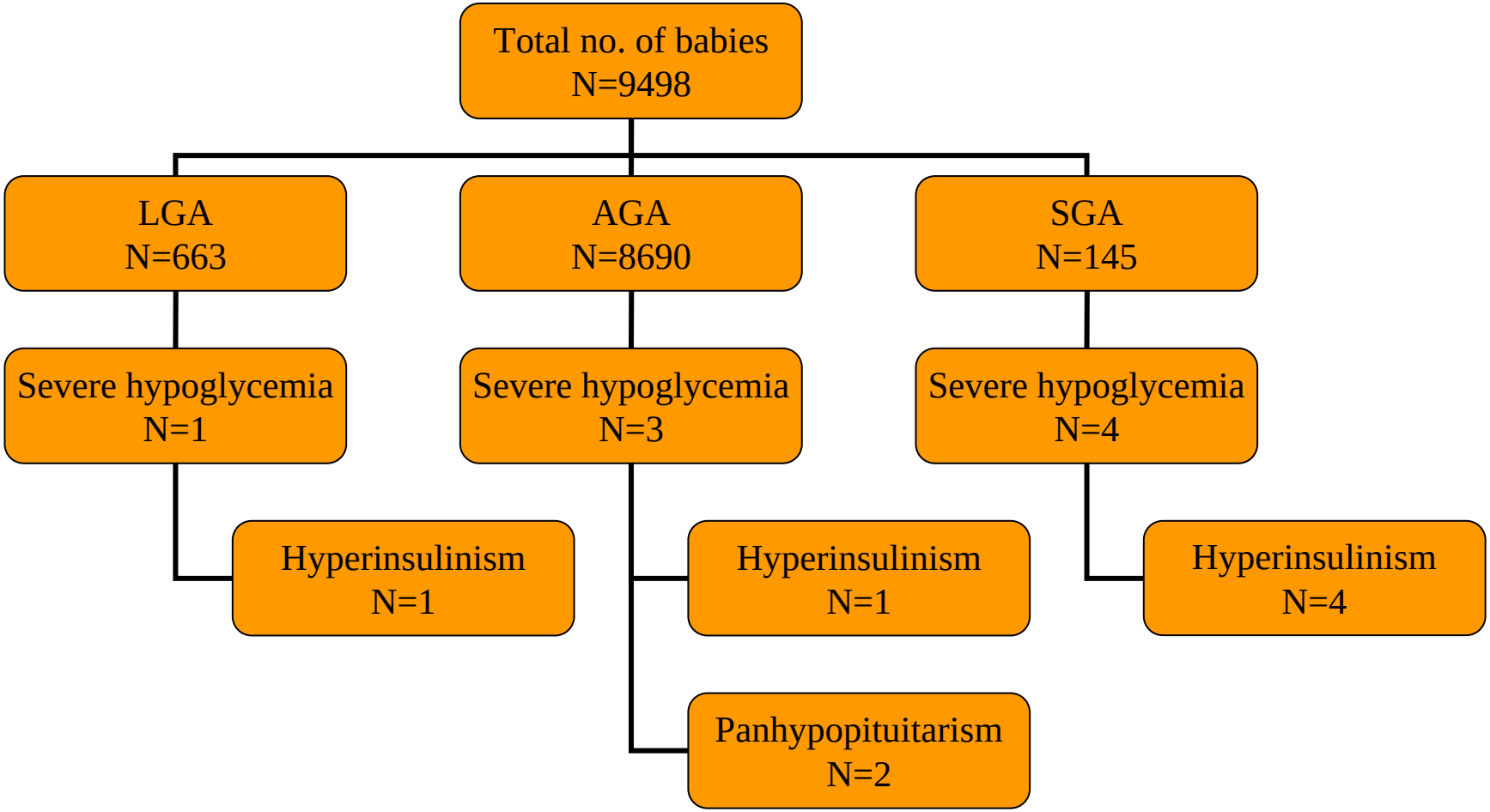
Results

- These babies had a mean gestational age and birth-weight of 38.8 (34-41)weeks and 2690(1240-4390)g respectively.
- The lowest blood glucose was <0.5mmol/l.
- All 8 babies were diagnosed with severe hypoglycaemia within first 24 hours of birth.
- Earliest time of initial diagnosis of severe hypoglycaemia was 2 hours after birth.
- Number of hypoglycaemic episode varied from 1 to > 5 in each baby.
- Of the 8 babies only one baby was born to Gestational Diabetic diet controlled mother, 4 were SGA, 1 LGA and 2 AGA .

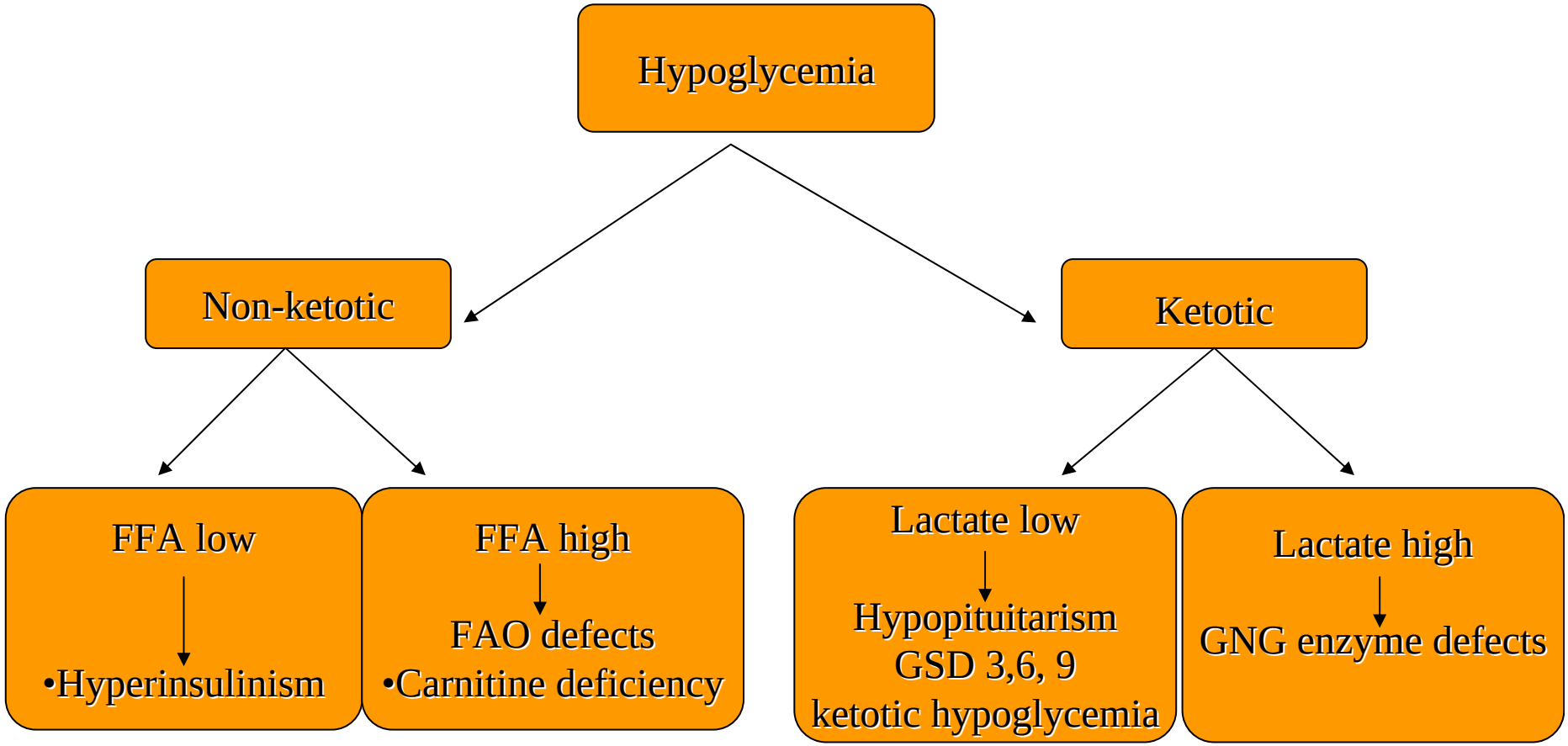
Results

- All 8 babies required intravenous glucose to treat initial episodes of hypoglycemia.
- 2 babies with persistent hyperinsulinaemic hypoglycemia required glucagon and hydrocortisone in addition to glucose (>12.5mg/kg/min), were transferred to tertiary perinatal centre for management.
- 4 babies with transient hyperinsulinaemic hypoglycemia required 6-8mg/kg/min glucose to treat hypoglycemia for 1 to 3 days
- 2 babies with pan-hypopitutarism hypoglycemia were consulted with endocrinologist and treated initially with hydrocortisone, and later required thyroxine and growth harmone replacement.
- At the time of discharge all 8 babies had normal neurological examination and had no ill effect of hypoglycemia.

Results


Total no. of babies
N=9498
LGA
N=663
AGA
N=8690
SGA
N=145
Severe hypoglycemia
N=1
Severe hypoglycemia
N=3
Severe hypoglycemia
N=4
Hyperinsulinism
N=1
Hyperinsulinism
N=1
Hyperinsulinism
N=4
Panhypopituitarism
N=2

Flow chart


Hypoglycemia
Non-ketotic
Ketotic
FFA low
•Hyperinsulinism
FFA high
FAO defects
•Carnitine deficiency
Lactate low
Hypopituitarism
GSD 3,6, 9
ketotic hypoglycemia
Lactate high
GNG enzyme defects

Conclusion

- The overall incidence of severe Neonatal Hypoglycaemia in our otherwise well newborn baby population is 1/1187
  (0.8 per 1,000 live births).
- The incidence of Hyperinsulinaemic Hypoglycaemia in our newborn babies is 1/1583(0.6 per 1,000 live births).
- Hyperinsulinism is the most common cause of severe hypoglycaemia in our SGA babies.
- Hyperinsulinaemic hypoglycaemia can cause neurological injury, therefore it is important that it is diagnosed and treated early.

Conclusion

- This study also demonstrates that serious endocrine disorder such as Panhypopitutarism can be diagnosed very early in the newborn period, even when there is no external congenital midline anomaly when hypoglycaemia screening is implemented.
- The implementation of guidelines for neonatal hypoglycaemia screening helps in early identification of babies at risk of adverse outcome and contribute to clinical management .
- Long term follow-up of these infants for neuro-developmental assessment will help identify prognostic factors.