

Risk Factors for Hypoglycaemia with Hypothermia in Neonates: An Audit in a Level II Special Care Nursery

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ABSTRACT

Background and objective: Hypoglycaemia is a common metabolic disorder in newborns. The aims of this retrospective study were to identify modifiable risk factors for hypoglycaemia and review the evidence to introduce a common neonatal hypoglycaemia and hypothermia care bundle.

Method: This study is conducted and reported using the STROBE Statement Guideline. A retrospective audit was done on all neonatal admission to this level 2 Special Care Nursery (SCN) from 1st January 2018 to 31st December 2018. Neonates were included if they had a primary diagnosis of 'hypoglycaemia'. Neonates with other chief diagnosis were excluded (including prematurity and sepsis). Hypoglycaemia was defined as a blood glucose level (BGL) less than 2.6 mmol/L. Demographic data and risk factors were extracted from the medical records.

Results: The total number of SCN admissions during that period was 1020. A total of 105 infants met inclusion criteria (n=105). The mean BGL was 1.9 mmol/L. Risk factors of hypoglycaemia in the included sample identified were: maternal gestational diabetes mellitus (GDM) on diet control (13%) or insulin (29%), insulin dependent diabetes mellitus (IDDM) (2%), betablockers (2%), macrosomia (4%), and Small for gestational age (7%).

Temperature analysis revealed almost half of all hypoglycemic neonates (49.5%) were hypothermic with a temperature of below 36.5°C. 22.8% out of the sample group had temperature of below 36°C. Majority of these hypoglycemic hypothermic newborns (63%) were born via caesarean section.

Conclusion: Hypothermia is common in the newborns with hypoglycaemia. However, it is difficult to ascertain which the primary condition is. As a result of this audit a 'hypothermia hypoglycaemia care bundle' has been developed to reduce overall neonatal admissions to the nursery from hypoglycaemia and/or hypothermia.

Keywords: Neonates; Hypoglycaemia; Hypothermia; Glucose; Dextrose; Thermoregulation; Temperature

INTRODUCTION

Hypoglycaemia is a common metabolic disorder in term newborns [1]. The definition of hypoglycaemia in neonates however, remains controversial [1]. Incidents of neonatal hypoglycaemia varies widely depending on the threshold of Blood Glucose Level (BGL) used. One study showed more than 50% of 'at risk' neonates will develop hypoglycaemia within the first 24 hours of life [2]. Another study showed incidents of hypoglycaemia across all newborns varies between 38% in developing country and 18% in developed country [3]. The World Health Organization guideline defines hypoglycaemia as blood glucose level of less than 45 mg/dl (2.5 mmol/L) [4].

The recommended threshold for treatment, often referred to

as 'operational threshold' varies widely amongst different centres, ranging from <1 mmol/L [5] to 2.7 mmol/L [6]. Mode of treatment for neonatal hypoglycaemia is also variable with supplemental formula feeding, oral glucose gel and intravenous dextrose 10% infusion or bolus being practised in various centres. The threshold for each intervention, however, has not been studied or validated extensively. It has been shown that blood glucose level (BGL) of less than 2.6 mmol/L will increase the risk of corticospinal tract injury in the setting of neonatal encephalopathy by almost four folds and lower points of cognitive and language score at 1 year of age [7]. A study from New Zealand showed an association between hypoglycaemia (BGL<2.6 mmol/L) with an increased risk of poor executive function and visual motor function at 4.5 years old [2]. Most neonatal centres around Western Australia defined neonatal

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hypoglycaemia as blood glucose level of <2.6 mmol/L. In this regional level II nursery in Western Australia, hypoglycaemia is the second commonest cause of nursery admission throughout year 2018 and is defined as blood glucose level of below 2.6 mmol/L as per WHO.

Often, treatment of hypoglycaemia results in separation of the mother and baby and this poses a significant cause of interruption in achieving maternal-infant bonding and the establishment of breast feeding. Unnecessary admission to the nursery also incurs additional costs to the hospital and the health care system around that region.

Hypothermia definition on the other hand, has been widely accepted as body temperature of below 36.5 centigrade (°C) in accordance to WHO definition [8]. Although hypothermia has been recognized as one of the risk factor for hypoglycaemia in neonates, it can also be a late sign of hypoglycaemia [5]. The true incident of isolated hypothermia in a term infant has not been ascertained in this centre. In a systematic review, it has been shown that incident of neonatal hypothermia ranges from 32%-85% even in tropical country and it is commonly associated neonatal death worldwide [8]. Various risk factors such as low ambient temperature, low gestation, low birth weight, birth asphyxia, low socioeconomic status and sepsis have been associated with hypothermia [8].

Given the importance of the diagnosis of hypoglycaemia and its potential short- and long-term complications, this study aims to investigate the common risk factors of hypoglycaemia and its association with hypothermia in this regional level II SCN in Western Australia.

METHOD

This study was done in a regional health centre with an annual delivery rate of around 3500 per year. The level II special care nursery (SCN) cares for newborn infants from 32 weeks of gestation. The annual number of SCN admissions over the last 3 years ranges from 956 to 1020 per year.

Newborn's blood glucose level (BGL) monitoring was done via heel prick and analysed by 'ABL90 flex' blood gas analyser. This method is on par with the Integra 400 chemical analyser (plasma) that uses the hexokinase method [9]. According to the centre guidelines, only newborns with risk factors for hypoglycaemia will have their blood glucose monitored after delivery. These risk factors include infant of diabetic mother, low birth weight (<2.5 kg), macrosomia >4.5 kg, preterm, maternal drugs (eg. beta blockers) and Maternal BMI >35.

There is an admission database for the Special Care Nursery (SCN). All newborns admitted to the SCN from January to December 2018 with the chief diagnosis of 'hypoglycaemia' were identified from the SCN database and included in the audit. All neonates born beyond 37 weeks of gestation with lowest BGL of less than 2.6 mmol/L were included. By applying such inclusion criteria, all neonates admitted to the nursery with other chief diagnosis were excluded; these include prematurity, respiratory distress, sepsis and others. Although some of them might have developed hypoglycaemia as a secondary diagnosis, our primary aim was to investigate risk factors of hypoglycaemia in a term neonate and to investigate its association with hypothermia as this

may be the main modifiable risk factor for hypoglycaemia in this group of newborn.

Out of these neonates, case notes were reviewed and newborns with lowest BGL of \leq 2.6 mmol/L were recruited as our main study sample group while newborns with lowest BGL of above 2.6 mmol/L were excluded. The relevant data of these infants were extracted from the case notes, these include: birth weight, gestation, gender, mode of delivery, lowest blood glucose level with time of age during that episode, maternal risk factors (diabetes or medication), temperature on nursery admission, intervention before and after nursery admission, any recurrent hypoglycaemia (defined by three or more episodes of hypoglycaemia), and results of hypoglycemic screen if done.

The proportion of newborns who presented to nursery with associated hypothermia was investigated. With this information, further analysis of the mode of delivery of these newborns was done and other possible risks of hypoglycaemia with hypothermia were examined. Subgroup analysis of the excluded sample was done.

Due to the significant proportion of hypoglycemic neonates presented with hypothermia upon nursery admission, a common 'hypoglycaemia-hypothermia' care bundle was introduced throughout year 2019. This would be the first common care bundle to be introduced in a nursery in Western Australia. A prospective study will be planned as part of the follow up study for this project in the future.

RESULTS

Total number of admissions to the Special Care Nursery (SCN) for year 2018 was 1020. 129 newborns with primary diagnosis of "hypoglycaemia" were screened from the nursery admission database, indicating a 12.6% overall admission rate to the SCN for 'Neonatal Hypoglycemia'. A total of 105 was included as the main study sample (n=105). 24 were excluded as their lowest PGL was above 2.6 mmol/L. These mainly consisted of newborns with maternal risk factors for hypoglycaemia and were 'prophylactically' admitted to the SCN for blood sugar monitoring and were given the diagnosis coding of 'hypoglycemia'.

The mean BGL of the included sample was 1.9 mmol/L (95% CI 1.7-2.1) with a mean gestation of 38 weeks 2 days.

The main risk factors for hypoglycaemia identified from the sample group were: Maternal Gestational Diabetes Mellitus (GDM) on diet control (13%) or on insulin (29%), Insulin Dependent Diabetes Mellitus (IDDM) (2%), betablockers (2%), macrosomia (4%), and Small for gestational age (7%) (Table 1). Forming part of the exclusion criteria, neonates with other chief diagnosis like prematurity and sepsis were excluded and hence not picked up as risk factors of hypoglycaemia in this study.

Table 1: Risk Factors for Hypoglycaemia.

Risk factors	Number (%)
Gestational Diabetes Mellitus (GDM) on diet control	14/105 (13%)
GDM On insulin	30/105 (29%)
Insulin Dependent Diabetes Mellitus (IDDM)	2/105 (2%)
Macrosomia (>4.5 kg)	4/105 (4%)
Betablockers	2/105 (2%)
On long term steroids	1/105 (1%)
Low birth weight (BW<2500 g)	7/105 (7%)

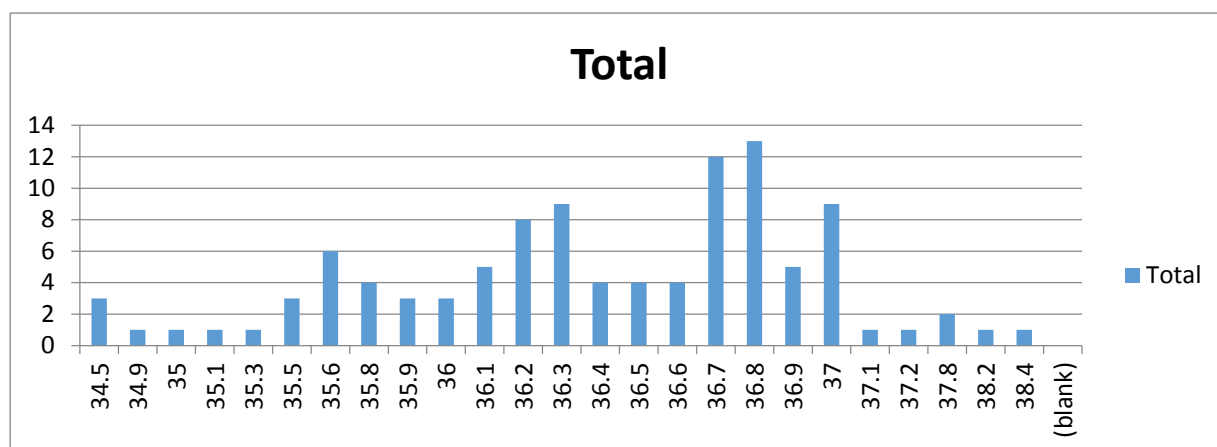


Figure 1: Temperature distribution of hypoglycaemic neonates. (X axis: Temperature, Y axis: Number of hypoglycaemic neonates).

Temperature analysis revealed almost half of the hypoglycaemic newborns were hypothermic with temperature of below 36.5°C (49.5%) with about 22.8% of them with temperature below 36°C upon nursery admission (Chart 1 and Table 2).

Table 2: Characteristic of included sample and proportion with hypothermia.

Total sample, n=105	
Mean Gestation	38 weeks 2 days
Male : Female	52:53=1:1
Mean Birth weight	3357.5 g (95% CI: 3235-3479 g)
Mean Blood Glucose Level (BGL)	1.9 mmol/L (95% CI 1.7-2.1)
Lowest BGL onset time, mean: 4 hours	85% within first 6 hours of life
<u>Temperature Analysis:</u>	
Mean Temperature:	36.3 C° (95% CI 35.5-37.1°)
Temp<36.5 (%)	51/105 (49.5%)
Temp 36-36.5	27/105 (26.7%)
Temp<36 C	24/105 (22.8%)

63% of the 'hypothermic hypoglycemic' newborns were born via caesarean section with equal proportion of them with or without maternal risk factors for neonatal hypoglycaemia (Table 3).

Table 3: Mode of delivery of the hypoglycaemia neonates.

Mode of delivery	Number (%)
Spontaneous vaginal delivery (SVD)	30/105 (29%)
Instrumental assisted	12/105 (11%)
Elective caesarean section	34/105 (32%)
Emergency caesarean section	29/105 (27%)

The 2 × 2 table showed the proportion of hypoglycaemia was higher (92%) in the severe hypothermic group compared to the mild hypothermic group (83%) (Tables 4 and 5).

Table 4: 2 × 2 table showing Mild Hypothermia 36°C-36.5°C and Hypoglycaemia.

		Hypothermia (36-36.5)	
		No	Yes
Hypoglycaemia (BGL<2.6 mmol/L)	No	14	10
	Yes	53 (79%)	51 (83%)

Table 5: 2 × 2 table showing hypothermia <36°C and hypoglycaemia.

		Hypothermia (<36)	
		No	Yes
Hypoglycaemia (BGL<2.6 mmol/L)	No	22	2
	Yes	81 (78%)	23 (92%)

Majority of the hypoglycaemia neonates (60%) received only supplemental formula feeding as their mode of treatment for their hypoglycaemia. All neonates admitted to the SCN were placed under a warmer from admission time and their temperature normalised as soon as possible.

It was noted that out of the 63 neonates who received formula feeding as their only mode of therapy, only 2 developed multiple episodes of hypoglycaemia (3%) as compared to the group that received IV therapy (9%) (Table 6).

Table 6: Treatment approach

Mode of therapy	Number (%)
Supplemental feed with formula milk	63/105 (60%)
Maintenance IV fluid with Dextrose 10%	15/105 (14%)
Bolus only (dextrose 10% 2 mls/kg)	4/105 (4%)
Bolus+maintenance IV fluid Dextrose 10%	23/105 (22%)

SUBGROUP ANALYSIS OF EXCLUDED SAMPLE: (NORMOGLYCEMIA)

19 out of 24 of the excluded samples were admitted for BGL monitoring in the nursery due to risk factors identified during delivery (mainly maternal GDM on insulin). It was the clinician's personal preference to have such newborns admitted to the nursery

for BGL monitoring. Interestingly, none of them developed hypoglycaemia. Although 9 out of 19 had temperature of 36-36.5°C upon nursery admission, none of them had temperature of below 36°C and none developed further hypothermia. Based on this subgroup's information and data, it can be postulated that with the correct temperature control and the liberal usage of formula top up feeding in such infants, the incident of neonatal hypoglycaemia could be reduced significantly. The sample size of the excluded sample was however too small for any statistical analysis.

DISCUSSION

In this regional level II nursery in Western Australia, hypoglycaemia was the second commonest cause of nursery admission for newborns after prematurity. It poses a significant cause of interruption to achieving maternal-infant bonding and breast-feeding establishment.

In this study, the incidents of hypothermia in the hypoglycemic newborns was almost 50% and almost a quarter of them had temperature of <36°C upon nursery admission.

More than half of these hypoglycemic and hypothermic newborns (63%) were born via caesarean section (Table 3). In this group of newborns, about 54% of them had maternal risk factors for hypoglycaemia, another 46% without. One could debate that the lower ambient temperature in the theatre may have contributed to the newborns being more hypothermic than newborns born via SVD in the birth suites upon nursery admission, it was however, difficult to prove that retrospectively. According to WHO recommendation, maternity operation theatre ambient temperature should be set at 25-28 [10] which was difficult to comply in most theatre [10].

Having skin to skin as soon as feasible should still be the priority. It should, however, be done correctly with at least two warm linen over the baby and mother. Having the appropriate skin to skin contact can prove to be challenging in the theatre when mother is still on the table. In a study published in 2017, it was noted that early skin to skin contact has been shown to reduce incidence of neonatal hypoglycaemia [11]. There are also reports of newborns becoming apneic on mother's chest during skin to skin due to various reasons, hence close monitoring of these newborns are imperative during the initial postnatal period [12].

It is uncertain if hypothermia was in fact, a major modifiable risk factor for this group of neonates who were born via caesarean section to develop hypoglycaemia. A 'Neonatal hypothermia and hypoglycaemia common care bundle' was since introduced in this centre and a repeat audit will be carried out in the near future (Chart 2).

- Temperature in Theatre to be set at: 23-25°C for caesarean section (WHO guideline)
- Resuscitation cot to be turned on when theatre is assigned for the Caesarean section (set at 75% output instead of default of 25%)
- Sterile linen on resus cot should be warmed prior to baby being born
- If baby is well, to have Identification bands and Intramuscular vitamin K immediately. A quick day 1 check to be done followed

by wrapping baby with two warm towels and a cap.

- Not to unwrap baby unless for skin to skin.
- To have skin to skin as soon as feasible with at least two warmed towels over the newborn during skin to skin
- To have weighing scale in OT available and admit newborns with BW <2.5 kg to SCN
- To have formula milk or glucogel ready in the OT/Birth Suite for at risk neonates.

Chart 2: Proposed hypoglycaemia and hypothermia common care bundle

CONCLUSION

Hypothermia in the hypoglycemic neonates was not uncommon. It is difficult to prove if hypothermia was a cause or an effect of hypoglycaemia from this study. It is imperative to have optimum thermoregulation in all neonates to avoid any possible neonatal complication.

LIMITATION

One major limitation to this study was the small sample size.

Other limitation was the temperature measurement method may be variable.

The subgroup analysis of the excluded group sample size (n=19) is also relatively small compared to the main sample of 105.

STATEMENT OF ETHICS

This study has ethics approval from the Human Research Ethics Committee of Joondalup Health Campus with the approval number of 1914.

AUTHOR CONTRIBUTIONS

Dr Chia Saw initiated and proposed the study, applied for ethics approval, finalised study protocol, extracted the data, completed the manuscript and submitted to journal for publication.

Dr Jason Tan supervised the process, provided expert opinion and finalised the common care bundle.

Dr Ravisha Srinivasjois analysed the data and provided statistical support.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

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REFERENCES

1. Kallem, V.R, A Pandita, G. Gupta. Hypoglycemia: when to treat? Clin Med Insights Pediatr. 2017;11:1179556517748913.
2. McKinlay CJD, Alsweiler MJ, Anstice SN, Burakevych N, Chakraborty A, Chase GJ, et al. Association of neonatal glycemia with neurodevelopmental outcomes at 4.5 years. JAMA Pediatr. 2017;171:972-983.

3. Pal DK, Manandha DS, Rajbhandari S, Land MJ, Patel N, Costello LDMA. Neonatal hypoglycaemia in nepal 1: Prevalence and risk factors. *Arch Dis Child Fetal Neonatal Ed.* 2000; 82: F46-F51.
4. Achoki R, Opiyo N, English M. Mini-review: Management of hypoglycaemia in children aged 0-59 months. *J Trop Pediatr.* 2010; 56: 227-234.
5. Levene I, Wilkinson D. Identification and management of neonatal hypoglycaemia in the full-term infant (British association of perinatal medicine-framework for practice). *Arch Dis Child Educ Pract Ed.* 2019; 104: 29-32.
6. Thornton PS, Stanley AC, Leon DDD, Harris D, Haymond WM, Hussain K, et al. Recommendations from the pediatric endocrine society for evaluation and management of persistent hypoglycemia in neonates, infants, and children. *J Pediatr.* 2015;167:238-245.
7. Tam EWY, Haeusslein AL, Bonifacio LS, Glass CH, Rogers EE, Jeremy JR, et al. Hypoglycemia is associated with increased risk for brain injury and adverse neurodevelopmental outcome in neonates at risk for encephalopathy. *J Pediatr.* 2012; 161: 88-93.
8. Lunze, K, Bloom ED, Jamison TD, Hamer HD. The global burden of neonatal hypothermia: systematic review of a major challenge for newborn survival. *BMC Med.* 2013; 11: 24.
9. Pelletier O, Arratoon C. Precision of glucose measurements in control sera by isotope dilution/mass spectrometry: Proposed definitive method compared with a reference method. *Clin Chem.* 1987;33:1397-1402.
10. Sultan P, Habib A, Carvalho B. Ambient operating room temperature: Mother, baby or surgeon? *Br J Anaesth.* 2017; 119: 839.
11. Chiruvolu A, Miklis KK, Stanzo C, Petrey B, Groves GC, McCord K, et al. Effects of skin-to-skin care on late preterm and term infants at risk for neonatal hypoglycemia. *Pediatr Qual Saf.*2017; 2: e030
12. Bohnhorst B, Gill D, Dordelmann M, Peter SC, Poets FC. Bradycardia and desaturation during skin-to-skin care: no relationship to hyperthermia. *J Pediatr.* 2004; 145: 499-502. Satici B, Gocet-Teki E, Engin Deniz, M Satici SA. Adaptation of the fear of COVID-19 Scale: Its association with Psychological distress and life Satisfaction in Turkey. *Int J Ment Health Addict.* 2020.