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PROFILE OF RISK FACTORS AND OUTCOME OF HYPOGLYCEMIA IN NEWBORNS ADMITTED IN THE NEONATAL UNIT OF A TERTIARY CARE HOSPITAL, ASRAM, WEST GODAVARI DISTRICT

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ABSTRACT: AIMS: 1. To know the various risk factors of neonatal hypoglycemia and their incidence among the babies admitted in tertiary care hospital, ASRAM, Eluru. 2. To know the outcome of neonatal hypoglycemia in both symptomatic and asymptomatic newborns in tertiary care hospital, ASRAM, Eluru. **DESIGN:** Prospective study. **SETTING:** Tertiary hospital based study over 24 months. **METHODS:** Blood glucose values are measured using Reagent Strip method (Glucotrend2 of USA. and confirmed by Laboratory Diagnosis The blood glucose values were measured at 1, 2, 4, 6, 12, 24, 36, 48 and 72 hours of life or till discharge whichever is earlier. **RESULTS:** A total of 150 cases were observed of which 59 cases (33.3%) developed hypoglycemia. The common risk factors observed are low birth weight in 23(46%), sepsis in 12(24%), IDM in 5 (10%), asphyxia in 4(8%) and 6 cases (12%) have no risk factors. 76.9% of the cases have developed hypoglycemia at the first hour of life. In our study 52% of neonates with hypoglycemia have recovered well with oral feeds given at 30mins. The remaining 48% required glucose infusion. Only 1 case had recurrent hypoglycemia (2%) even on glucose infusion and it is controlled with single dose hydrocortisone. **CONCLUSIONS:** Hypoglycemia is a common in the newborns, and a high index of suspicion is required to identify it early. It is also an easily treatable problem, in most occasions. Hypoglycemia in the newborn if detected and treated early will prevent adverse neurodevelopmental outcome. **KEYWORDS:** hypoglycemia, low birth weight, risk factors, neurodevelopment.

INTRODUCTION: Hypoglycemia is a common disorder in neonates.^{1,2} In neonates there is not always an obvious correlation between blood glucose concentration and the classic clinical manifestation of hypoglycemia. The absence of symptoms does not indicate that glucose concentration is normal. There is still no universal definition for this disorder.³

The definition of clinically significant hypoglycemia is one of the most confused and contentious issue in contemporary. Koh et al did a detailed survey and found that the definition ranged from 18 mg/dl to 72mg/dl. Confusion exists due to the fact that the "normal" range of blood glucose is different for each newborn and depends upon a number of factors including birth-weight, gestational age, body stores, feeding status, availability of energy sources as well as the presence or absence of disease. Thus the definition of hypoglycemia should be flexible and encompass all these aspects. Further, there is no concrete evidence to show the causation of adverse long-term outcomes by a particular level or duration of hypoglycemia.⁴

A recent consensus has been to evolve an "operational threshold". This threshold is currently believed to be a blood glucose value of less than 40 mg/dl (plasma glucose less than 45 mg/dl). Many

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authorities now urge that any value of blood glucose less than 50mg/dl in neonates be viewed with suspicion and vigorously treated.⁵

Hypoglycemia is one of the most common clinical care issues facing the neonatal practitioner⁶. Neonatal hypoglycemia may cause many acute and chronic complications and may be observed in infants with no clear factors, it may cause posterior cerebral lesions, abnormal findings, at neurologic examination, and symptomatic epilepsy, most frequently occipital lobe epilepsy.⁷ Estimates of the incidence of hypoglycemia in the newborn depend both on the definition of the condition and the methods by which blood glucose concentrations are measured. The overall incidence has been estimated at 1 to 5 per 1,000 live births, but it is higher in at-risk populations. For example, 8% of large-for-gestational-age infants (primarily infants of diabetic mothers [IDMs]) and 15% of preterm infants and infants who have intrauterine growth retardation (IUGR) have been reported as having hypoglycemia; the incidence in the entire population of "high-risk" infants may be as high as 30%.

Recurrent episodes of neonatal hypoglycemia are strongly associated with long term physical and neurodevelopmental deficits. Moreover in neonates hypoglycemia can be overlooked as it may have non-specific symptoms only.

This study was therefore carried out to analyse the risk factors associated with neonatal hypoglycemia and to evaluate the outcome of the infants with neonatal hypoglycemia.

Neonatal hypoglycemia, independent of HIE, has been associated with adverse outcome in both term and preterm infants.⁸⁻¹⁰ However, no conclusive evidence on the severity and duration of hypoglycemia causing brain damage has been reported.^{11,12} Basu et al showed that the degree of hypoglycemia was correlated to the severity of HIE in term asphyxiated newborns.

Neurologic morbidity occurs particularly in those infants who have suffered severe, protracted, or recurrent symptomatic hypoglycemia. Hypoglycemia combined with hypoxia-ischemia (asphyxia) is more deleterious to the immature brain than either condition alone. Hypoglycemia (blood glucose level <45 mg/dL), isolated or combined with mild hypoxia ischemia, is injurious to the newborn brain and must be monitored for closely and managed aggressively to avoid adverse consequences.¹³

Hypoglycemia has been associated with abnormal neurological outcomes but not with abnormal psychomotor development.¹⁴

The study by Burns et al¹⁰ also supports the notion that MRI should be a routine investigation for the newborn infant with symptomatic hypoglycemia to define the nature of any cerebral injury.

MATERIALS AND METHODS:

Study Period: The babies born in our hospital between 01-11-2010 to 31-10-2012 (over a period of 24 months) were included in this study.

Inclusion Criteria:

1. Babies with birth weight <1.8 kgs and are having risk factors.
2. Babies of diabetic mother.
3. Babies with h/o perinatal asphyxia.
4. Babies with birth weight >1.8kgs and presenting with signs and symptoms suggestive of hypoglycemia.
5. Babies with clinical sepsis.

Exclusion Criteria:

1. All babies with blood glucose value >40 mg/dl.
2. Babies with birth weight >1.8 kgs and had no risk factors with blood glucose value >40 mg/dl.

METHODS: Blood glucose values are measured using.

1. Reagent Strip method and confirmed by Laboratory Diagnosis.

a. Reagent Strips (Glucose Oxidase): Though widely used and are important 'point of care' method, they are unreliable especially, at blood glucose levels less than 40-50mg/dl. They are useful for screening purpose but low values should be always confirmed by formal laboratory analysis, before a diagnosis of hypoglycemia is made (however treatment must be instituted based on results of reagent strips). It is important to also consider the variations between capillary and venous, blood and plasma, and immediate and stored samples (whole blood sugar is 10-15% less than the plasma sugar, the glucose levels can fall by 14-18 mg/dL per hour in blood samples that await the analysis 19).

b. Laboratory Diagnosis: In the laboratory (lab), glucose can be measured by either the glucose oxidase (calorimetric) method or by the glucose electrode method (as used in blood gas & electrolyte analyser machine). Blood samples were analyzed immediately to avoid erroneously low glucose levels.

In a neonate the preferred site for capillary puncture is the heel. Site of puncture: Because the course of the plantar arteries and veins is on the medial aspect of the plantar surface of the heel, this is the preferred site for puncture however almost any place on the fleshy, uncalloused heel of the infant is suitable for blood collection. The more medial surface of the heel should be avoided as a precaution against scar formation, that might be a nidus of pain when the infant begins to walk.

RESULTS: In our study, Low birth weight has accounted for the maximum number of neonatal hypoglycemia that is in 23 cases (46%), followed by sepsis which was the cause in 12 cases (24%). IDM and asphyxia have accounted for the remaining risk factors and no risk factors were found in 6 cases (12%).

Risk Factors	No. of cases	Percentage
Low Birth Weight	23	46%
Sepsis	12	24%
IDM	5	10%
Asphyxia	4	8%%
No. Risk Factors	6	12%

Table No. 1: Frequency of Neonatal hypoglycemia in different Risk Factors

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Symptomatic cases are those whose blood glucose value $<40\text{mg/dl}$ and other causes were ruled out and presented with lethargy, refusal of feeds, apnea, irritability, excessive crying, tachypnea, hypothermia and seizures.

SYMPTOMS	No. of cases	Percentage
Asymptomatic	36	72%
Symptomatic	14	28%

Table 2: CLASSIFICATION OF HYPOGLYCEMIA

In a hypoglycemic baby with seizures all the other causes of seizures were ruled out and those controlled with glucose infusion, blood glucose $<40\text{mg/dl}$ at presentation are included in the study.

SYMPTOMS	No. of cases	Percentage
Lethargy & Refusal of Feeds	9	64.2%
Seizures	5	35.7%

Table 3: SYMPTOMATIC CLASSIFICATION OF HYPOGLYCEMIA

Low birth weight was the most common of all the risk factors of hypoglycemia, IUGR has accounted for the larger part of LBW babies with 57% of cases of LBW, and remaining 43% are due to prematurity.

Most of the babies developed hypoglycemia on the first day of life (52%).

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Time of Onset	No. of cases	Percentage
<24 hrs. of Life	26	52%
>24hrs of Life	24	48%

Table 4: ONSET OF HYPOGLYCEMIA (IN DAYS)

Among the 52% of cases who developed hypoglycemia on first day of life, 3/4th (i. e 77%) of cases developed hypoglycemia in first hour of life.

52% of babies with hypoglycemia recovered well with oral feeds only while 36% of babies required glucose infusion alone and 12% required both glucose infusion and drugs.

Treatment	No. of cases	Percentage
Oral Feeds	26	52%
Glucose Infusion	18	36%
Glucose Infusion & drugs	6	12%

Table 5: MANAGEMENT OF HYPOGLYCEMIA

Poor outcome is considered when the babies are having recurrent seizures for which all the other causes are ruled out and those requiring AEDs, H/O. Asphyxia triggering the seizures. Those with depressed activity, depressed reflexes, poor weight gain are considered as babies with poor outcome. 4 cases (66.67%) of poor outcome is due to asphyxia, 1 case (16.67%) is due to IDM (infant of diabetic mother) and in one case (16.67%) the poor outcome is attributed to IUGR (Intra uterine growth retardation).

Outcome	No. of cases	Percentage
Normal	44	88%
Poor	6	12%

Table 6: OUTCOME OF HYPOGLYCEMIA

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DISCUSSION: The present study is designed to study the risk factors of hypoglycemia and to assess the outcome of the neonate at discharge and at routine follow ups in our hospital, ASRAM, Eluru.

There are many studies done on knowing the incidence of risk factors of hypoglycemia in those particular hospitals and in those particular areas. One of such studies was done by Dorina Rodica Burdan et al Neonatal Hypoglycemia. The incidence of the risk factors in Salvador via obstetrics-gynecology hospital, ARAD. According to this study the neonates with neonatal hypoglycemia, after the screening test, were selected and found out that incidence of hypoglycemia is high in low birth weight babies and followed by perinatal hypoxia, hypothermia, respiratory distress, sepsis, neonatal shock and polycythemia.

Another similar study done by Sasidharan CK et.al in Institute of Maternal and Child Health, Medical College, Kozhikode, Kerala found out that eight variables strongly and independently predicted the risk of neonatal hypoglycemia, at least one being present in 89.1% of the hypoglycemic neonates. The risk factors included are Prematurity, low birth weight, maternal diabetes mellitus, delay in initiation of feeding for more than 2hrs post nately, maternal pre-eclampsia, and eclampsia, birth asphyxia, cold stress, or hypothermia, and maternal oligohydramnios.

D. Pal, et.al conducted a study on prevalence and risk factors of Neonatal Hypoglycemia in Nepal.

According to this study significant independent risk factors for moderate hypoglycemia included post-maturity, birth weight under 2.5kg, small head size, and raised maternal thyroid stimulating hormone.

A study conducted by Schafer et.al concluded that the most common associated risk factor was low birth weight followed by delayed feeding, birth asphyxia, and neonatal sepsis.

Studies by Srinivasan et.al, by Tanzer et.al emphasized that blood glucose values in the first three hours of life even of full term normal neonates can be lower than 40 mg/dl and were of the opinion that they may be physiological.

Study by Collins et.al pointed out that hypoglycemia in small for dates infant is due in part to hyperinsulinemia and this they pointed may lead to recurrence of hypoglycemia after the initial dip in glucose.¹⁵

Study by Schaffer et.al concluded that routine glucose testing is indicated in large-for-gestational age newborn infants of non-diabetic mothers. The 1-hour glucose value of the maternal oral glucose tolerance test is a fairly good predictor of subsequent neonatal hypoglycemia. A single elevated 1-hour value of ≥ 180 mg/dl markedly increases the risk of neonatal hypoglycemia.

Regarding the neurodevelopmental effects of hypoglycemia it was reviewed by Lucas et.al as early as 1988. Nowadays lot of emphasis is being given to the neuro-developmental effects of neonatal hypoglycemia, as it can be easily avoided by a simple screening test and by maintaining euglycemia.

Brain imaging findings in neonatal hypoglycemia: case report and review of 23 cases by Alkalay et.al published in Clin Pediatr.2005 concluded that abnormal brain imaging findings are associated with profound hypoglycemia and show involvement of the occipital lobes.¹⁶ Half of these infants had visual impairment and their median and range of plasma glucose values, and postnatal age when hypoglycemia was first detected were 7 mg/dl and 48 hours respectively.

Neonatal Hypoglycemic Brain Injury- A Common Cause of Infantile onset Remote Symptomatic Epilepsy by V Udani et al conclude that Neonatal Hypoglycemia is the most common etiology of remote symptomatic epilepsy.

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Duvanel et al in 1998 studied long-term effects of neonatal hypoglycemia on brain growth and development in small-for-gestational-age preterm infants concluded that recurrent episode of hypoglycemia were strongly correlated with persistent neurodevelopmental and physical growth deficits until 5 yrs. of age.¹⁷

Recurrent hypoglycemia was also a more predictable factor for long-term effects than the severity of a single hypoglycemic episode.

Therefore repetitive blood glucose monitoring and rapid treatment even for mild hypoglycemia are recommended for small-for-gestational-age infants in neonatal period.

Singh Met.al¹⁸ in 1991 studied on the neurodevelopmental outcome of asymptomatic & symptomatic babies with neonatal hypoglycemia concluded that the neurodevelopmental status of babies with symptoms other than seizures was also significantly poor when compared to asymptomatic hypoglycemic babies. The duration of hypoglycemia was directly related to the MDI.

Hypoglycemic Brain injury by Vannucci RC et.al published in Semin Neonatal 2001 suggested that Hypoglycemia combined with hypoxic ischemia (asphyxia) is more deleterious to the immature brain than either condition alone.¹⁹

A study by Tam EW et.al concluded that Neonatal hypoglycemia is associated with additional risks in the setting of neonatal encephalopathy with increased corticospinal tract injury and adverse motor and cognitive outcomes.²⁰

With the information available from the literature a study was designed to know the risk factors of hypoglycaemia prevalent in our hospital and the effect of hypoglycaemia on the neurodevelopmental outcome of the babies with hypoglycaemia. Based on this study a screening schedule is designed so that hypoglycemia can be detected at the earliest time and treat it accordingly to maintain euglycemic state in order to maintain the normal neurodevelopmental outcome of the neonate.

In this study all the newborn babies delivered in our hospital which comes under the high risk category like low birth weight, preterm, IUGR babies, birth asphyxia, IDM, LGA babies, neonatal sepsis were screened for blood glucose levels at a regular interval. The glucose monitoring is done by using glucose strips. If a very low glucose levels were obtained then a blood sample was sent to central lab simultaneously to know the plasma glucose. According to srinivasan et.al the glucose values are lowest with in the first 3hrs of life.

So, blood glucose levels of these high risk babies were measured at 30 mins, 1hr, 2nd hr, 4th hr, 6hrs, 12hrs, 24hrs, 48hrs, and 72 hrs of life

CONCLUSIONS:

1. The incidence of neonatal hypoglycaemia in our hospital is 33.3%.
2. The common risk factors of neonatal hypoglycemia in our hospital are low birth weight (46%), sepsis (24%), IDM (10%), Asphyxia (8%), & no risk factors (12%).
3. The incidence of each risk factor leading to hypoglycemia is low birth weight (47.9%), Asphyxia (44.4%), Sepsis (41.3%), & no risk factors (10.3%).
4. Hypoglycemia is a common problem in apparently normal asymptomatic babies. It is more consistently present when above mentioned risk factors exist.
5. Most of the cases developed hypoglycemia in the first hour of life, so screening for high risk neonates should be done at 1hr, 2hrs, 4hrs, 6hrs, 12hrs, 24hrs, 48hrs, and 72hrs of life or maintaining euglycemia with oral feeds.

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6. Mandatory blood glucose screening in babies with any of these risk factors serve as an easy and cost effective measure for identification of this condition.
7. Most of the cases with hypoglycemia maintained euglycemia only with oral feeds, so Oral feeds should be encouraged with in first hr. of life.
8. Mother should be counselled about the importance of breastfeeding.
9. Early treatment of hypoglycaemia will have normal neurological outcome of the baby.
10. Hypoglycemia contributes to abnormal neurodevelopmental outcome in infants who have other risk factors for brain injury, such as prematurity or hypoxic-ischemic brain injury.

REFERENCES:

1. Cornblath M. Neonatal hypoglycaemia 30 years later; does it injure the brain? Historical summary and present challenges. *Acta Paediatr Jpn* 1997; 39:S7-S11.
2. Wilker RE Hypoglycemia and hyperglycemia. In Cloherty JP, Stark AR peds. *Manual of neonatal Care*, 6th ed.pg:540-549.
3. Cornblath M, Hawdon JM, Williams AF, Aynsley-reef A, Ward- Platt MP, Schwartz et.al, Controversies regarding definition of hypoglycaemia: suggested operational thresholds. *Pediatrics* 2000; 105: 1141-1145.
4. Cornblath M, Schwartz R. Outcome of neonatal hypoglycaemia. *Br Med J*. 1999; 318:194.
5. Behrman, Kliegman, Stanton, Nelson textbook of paediatrics, 19th ed Saunders 2011.
6. Cowett PM, Long Ead J L. Neonatal glucose metabolism; differential diagnosis, evaluation, and treatment of hypoglycemia. *Neonatal Netw* 2002 Jun; 24-9.
7. Caraballo RH, Sakr D, Mozzi M et al. Symptomatic occipital lobe epilepsy following neonatal hypoglycemia. *Paediatric Neural* 2004 Jul31 (I); 24-9
8. Lucas A, Morley R, Cole TJ. Adverse neuro-developmental outcome of moderate neonatal hypoglycemia. *Br Med J* 1988; 297: 1304 -8.
9. Caraballo RH, Sakr D, Mozzi M et al. Symptomatic occipital lobe epilepsy following neonatal hypoglycemia. *Pediatr Neurol*. 2004; 31: 24-9. doi: 10.1016/j.pediatrneurol.2003.12.008
10. Burns CM, Rutherford MA, Boardman JP et al. Patterns of cerebral injury and neurodevelopmental outcomes after symptomatic neonatal hypoglycemia. *Pediatrics*.2008; 122:65-74.
11. Hawdon JM. Hypoglycaemia and the neonatal brain. *Eur J Pediatr*. 1999; 158 (Suppl 1):S9-S12.
12. Rozance PJ, Hay WW. Hypoglycemia in newborn infants: Features associated with adverse outcomes. *Biol Neonate*. 2006; 90 (2):74-86.
13. Terrie Inder. How Low Can I Go? The Impact of Hypoglycemia on the Immature Brain. *Pediatrics* 2008; 122; 440.
14. Brand PL, Molenaar NL, Kaaijk C et al. Neurodevelopmental outcome of hypoglycaemia in healthy, large for gestational age, term newborns. *Arch Dis Child*. 2005; 90:78-81
15. Srinivasan G et al. Plasma glucose values in normal neonates: A new look. *J Pediatr* 109:114, 1986.
16. Alkalay AL, Flores-Sarnat L, Sarnat HB, Moser FG, Simmons CF. Brain imaging findings in Neonatal Hypoglycemia: case report and review of 23 cases. *Clin pediatr (Phila)*. 2005 Nov-Dec; 44(9):783-90.

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17. Duvanel CB, Fawer CL, Cotting J, Hothfield P, Matthieu JM. Long term effects of neonatal hypoglycemia on brain growth and psychomotor development in small-for gestational age preterm infants. *J Pediatr*. 1999;134:492-8
18. Singhal PK, Singh M, Paul VK, Malhotra AK, Deorari AK, Ghorpade MD. A controlled study of sugar fortified milk feeding in prevention of neonatal hypoglycemia. *Indian J Med Res* 1991;94:342-5.
19. Vannucci RC, Vannucci SJ. Hypoglycemic Brain Injury, *Semin Neonatal* 2001 Apr;6 (2):147-55.
20. Tam EW, Haeusslein LA, Bonifacio SL, Glass HC, Rogers EE, Jeremy RJ, Barkovich AJ, Ferriero DM. Hypoglycemia is associated with increased risk for brain injury and adverse neurodevelopmental outcome in neonates at risk for encephalopathy. *J Pediatr* 2012 Jul; 161(1):88-93.

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