ejpmr, 2017,4(7), 497-502

SJIF Impact Factor 4.161

EUROPEAN JOURNAL OF PHARMACEUTICAL AND MEDICAL RESEARCH

www.ejpmr.com

Research Article

ISSN 2394-3211

EJPMR

STUDY OF MORBIDITY PATTERN OF HYPOGLYCEMIA IN NEONATES ADMITTED TO A TERTIARY CARE CENTER-AN EXPERIENCE OF TWO YEARS

Arakhita Swain*[1], Kedarnath Das[2], Suresh Kumar Tripathy[3], Saiprasanna Behera[4] and Saroj Kumar Satpathy[5]

[1*,2]Associate Professor, Department of Paediatrics, SCB Medical College, Cuttack, Odisha.
[3]Senior Resident, Department of Paediatrics, KIMS, Bhubaneswar, Odisha.
[4]Research Associate in Paediatrics, SCB Medical College and SVP PGIP, Cuttack, Odisha.
[5]Professor, HOD of Paediatrics, SCB Medical College, Cuttack, Odisha.

***Corresponding Author: Arakhita Swain**

Associate Professor, Department of Paediatrics, SCB Medical College, Cuttack, Odisha.

Article Received on 06/05/2017 **Article Revised on 27/05/2017** **Article Accepted on 17/06/2017**

ABSTRACT

Background: Hypoglycemia, the most common metabolic abnormality in neonates, is associated with neuronal damage and death especially when it occurs during the 1st few days of life. It is a common co-morbid condition associated with prematurity, birth asphyxia, IUGR, IDM, sepsis, various inborn errors of metabolism and endocrine disorders. The present study was conducted in SNCU of SCB Medical College and SVP PGIP, Cuttack over a period of two years with an aim to study the incidence, various clinical features, different risk factors (maternal and neonatal) as well as the morbidity and mortality pattern associated with neonatal hypoglycemia. ***Materials and Methods:*** It was a hospital based prospective observational study including 218 neonates at risk for hypoglycemia. All the babies were screened for hypoglycemia and blood samples were sent to the laboratory for confirmation of blood glucose. All the data were analysed statistically with Med Calc. ***Results:*** The incidence of hypoglycemia was 7.87% with a male preponderance i.e. 1.11:1 and more babies were delivered vaginally. The LBW (both preterm and Term SGA) babies contributed the maximum towards the incidence of hypoglycemia (55.50%) followed by Prematurity as an independent factor (48.60%), Birth asphyxia (38.07%) and SGA (14.22%) and it increased further with co-existence of two risk factors. The commonest clinical presentation was jitteriness and tremor followed by lethargy, poor feeding. Majority cases were discharged and death occurred in 7.80% while some babies were discharged with some sequelae. ***Conclusion:*** Neonatal hypoglycemia not only can cause mortality, but also may lead to serious neurological damage in newborn period. Early detection and prompt correction of hypoglycemia before occurrence of symptoms is the most important in the first step of management, but, for definite treatment the management of underlying cause is the second important and highly essential step.

KEYWORDS: Neonatal hypoglycemia, metabolic abnormality, neurological damage.

INTRODUCTION

Hypoglycemia, the most common metabolic abnormality in neonates, is associated with neuronal damage and death especially when it occurs during the 1st few days of life. This common co-morbid condition is associated with prematurity, birth asphyxia, intrauterine growth retardation, infants of diabetic mother, sepsis, various inborn errors of metabolism and endocrine disorders. Neonatal hypoglycemia represents an urgent diagnostic and therapeutic challenge that must be answered promptly to avoid the adverse consequences of hypoglycemia, most importantly damage to CNS leading to abnormal neurodevelopmental outcome, decreased overall IQ, reading and learning ability, arithmetic proficiency and motor performance over long term.[1] Among various neonatal hazards, the risk of neonatal hypoglycemia is one that is often underestimated. With growing interest in metabolism during neonatal period, neonatal hypoglycemia has been recognized as a definite clinical entity. Nevertheless, controversy still surrounds the definition, significance and management of neonatal hypoglycemia. Moreover, the introduction in the early 1970s of reagent strip glucose assay (e.g. Dextrostix Tm) for cot side screening of newborns at risk, led to clinical classification of neonatal hypoglycemia.[2,3] Clinical experiences say that hypoglycemia leading to neonatal death is very common in our state but; there is paucity of studies as well as literatures on Neonatal Hypoglycaemia. The present study was done to know the morbidity pattern in newborn at risk for hypoglycemia at newborn care centre of S.C.B. Medical College and SVPPGIP, Cuttack.

AIMS AND OBJECTIVES

1) To study the incidence, various clinical features and association of different risk factors (maternal and neonatal) with neonatal hypoglycaemia, 2) To study the morbidity and mortality pattern associated with it. 3) To

establish how early diagnosis and timely effective interventions will decrease the mortality and morbidity due to hypoglycaemia and 4) To know how the treatment of the underlying associated causes will be helpful.

MATERIALS AND METHODS

This hospital based prospective, observational study was conducted in SNCUs of SCB Medical College and SVP PGIP, Cuttack, over a period of two years extending from October 2013 to October, 2015. All the INBORN at risk neonates susceptible for hypoglycemia and screened to have low blood glucose level (<40 mg/dL according to operational threshold definition) were taken for study. A total of 218 cases with low blood glucose level met the

Inclusion Criteria:-

a) Inborn neonates
b) At risk neonates for hypoglycaemia
i) LBW babies (<2.5 kg),
ii) Preterm babies (<35 wks. of gestation),
iii) SGA & LGA infants,
iv) Infant of diabetic mother (IDM),
v) Infants with Rh-hemolytic disease,
vi) Infants born to mothers receiving therapy with Terbutalin / propranolol / labetalol / oral hypoglycemic agents and vii) Infants with morphological IUGR and
c) Any sick neonate (infants with sepsis, asphyxia, shock during active phase of illness).

Exclusion Criteria:- **a)** Outborn babies, b) Any baby who could not be followed up till improvement or death, c) Baby with congenital malformations, d) Babies of >28 days old, e) Infants on IV dextrose therapy before screening for hypoglycaemia and f) Denied for consent. Detailed history of all cases was taken giving due importance to maternal factors such as age, parity, history of gestational diabetes, hypertension, infection, medication like corticosteroid therapy, obstetric complications like fetal distress, mode of delivery and natal history such as APGAR scores, resuscitation, birth weight, gestational age were recorded in predesigned proforma (given below).

All neonates after admission were screened for blood glucose level at 2, 6, 12, 24, 48 and 72 hours. The blood glucose level was screened by glucometer and confirmed in laboratory by glucose-oxidase method and other relevant investigations were done to diagnose the co-morbidities associated with hypoglycemia. Statistical data was mentioned regarding the number of admissions, cause of admission and morbidities which were associated with hypoglycemia. All the babies were followed up till discharge or death for outcome. All the data were analysed statistically with MedCalc.

RESULTS

There were altogether 218 neonates with hypoglycaemia out of total 2770 newborns admitted (7.87%) with male preponderance (M: F=1.11:1) and more babies (80%) delivered vaginally.

The LBW (both preterm and Term SGA) babies contributed the highest towards the incidence of hypoglycemia (55.05%) followed by Prematurity (48.16%), Birth asphyxia (46.33%) and SGA (14.22%) as independent factors. (**Table-1, 2, 3**) All 8 neonates with IEM had hypoglycaemia. The incidence of hypoglycemia increases with increased of severity of HIE (6.79%, 13.35% and 22.0% in HIE-I, HIE-II and HIE-III respectively) which is statistically significant. (**Table-2**).

Some babies had multiple associated conditions suggesting further increased incidence of hypoglycaemia with two combined risk factors (Pre-term +SGA 43.24% and Pre-term +RDS 23.24%). (**Table-4**) Maternal anemia (Hb <10gm %), Prolonged Labour, Low maternal Age (16-20 yrs) and Maternal Fever (Mostly 3rd trimester) were common antenatal factors associated with Neonatal Hypoglycaemia (37.61%, 24.77%, 21.1% and 11.92% respectively). (**Table-5 and 6**).

Ninety (41.28%) neonates with Hypoglycaemia were symptomatic whereas, rest 128 (58.72%) were asymptomatic. Jitteriness and Tremor**,** Lethargy and Poor Feeding, Tachypnea and Cyanosis with Apnea were common clinical features. (**Table-7**) Majority (94.04%) of Neonatal Hypoglycaemia were transient and rest 5.96% were persistent.

In 12.38%, 54.59%, 16.51% and 28.90% cases of Neonatal Hypoglycaemia, the onset was within 2 hours, within 24 hours, on day-2 and on Day-3 after birth respectively. (**Table-8 and 9**) Initial low blood glucose values of asymptomatic patients range from 22 to 36 with a mean of 28.20 ± 7.9, whereas initial blood glucose values of symptomatic patients ranges from 12 to 21 with a mean of 17.90 ± 4.89. At 72 hrs after IV glucose therapy & feeding, the blood glucose values ranged from 42 to 67 with a mean of 48.32 ± 9.3 in asymptomatic & 28 to 46 with a mean of 44.30 ± 7.3 in symptomatic cases, with 13 babies still having low blood glucose level after 72 hours of life. (**Table-10**) Majority (62.22%) of all symptomatic hypoglycemic NBs have blood sugar levels in the range of 11-20 mg/dl. (**Table-11**)

In the present study, 91.28% of all hypoglycemic cases were discharged, death occurred in 7.80% of cases, while 2 cases were referred to other departments for further management. Some babies were discharged with some sequelae. (**Table-12**).

Table-1: **Incidence of Hypoglycemia (N=218) in Different Neonatal Conditions**

Neonatal conditions	Total	Hypoglycemia	Percentage of Total
Birth asphyxia	923	101	10.94%
Sepsis	720	55	7.63%
Preterm (includes preterm SGA)	893	105	11.75%
Term SGA	97	15	15.46%
Preterm SGA	37	16	43.24%
Suspected IEM	8	8	100%
IDM	21	10	47.61%
RDS	14	4	28.57%
LBW (1.5-2.5kg)	557	45	8.07%
VLEW (1-1.499 Kg)	301	37	12.3%
ELBW (<1 Kg)	123	38	30.89%

Table-2: Gradation of HIE and association of Hypoglycaemia

Grading of HIE	Total Number of HIE cases	No. of hypoglycemia associated with HIE	P-value
HIE-I	471 (51.02%)	32 (6.79%)	=0.0001
HIE-II	352 (38.1%)	47 (13.35%)	
HIE-III	100 (10.83%)	22 (22.0%)	

Table-3: Association of LBW and Hypoglycaemia (n=218)

Criteria	Hypoglycemia (Percentage)	NonHypoglycemia	Total	P-value
LBW	120 (55.05)	981	1101	<0.0001
Normal birth weight	98 (44.95)	1571	1669	
Total	218	2552	2770	

Table-4: Two Risk Factors and N Hypoglycaemia (Nn=218)

Parameters	Total	Hypoglycemia	Percentage of Total
Preterm with SGA	37	16	43.24%
Preterm with sepsis	218	40	18.34%
Preterm with BA	140	18	12.85%
Term SGA with BA	66	11	16.66%
Term SGA with sepsis	19	4	21.05%
Preterm RDS	13	3	23.07%

Table-5: Antenatal Factors and Hypoglycaemia (n=218)

Condition	No. of Hypoglycemia	Percentage of Total
Maternal anemia Hb <10gm%	82	37.61
Prolonged Labour	54	24.77
Low maternal Age (16-20 yrs)	46	21.1
PROM	32	14.67
Maternal Fever (Mostly 3rd trimester)	26	11.92
eclampsia & eclampsia	13	5.96
APH	10	4.58
Gestational DM & Pre Gestational DM	10	4.58
UTI	3	1.37

Table-6: Maternal Anaemia and N Hypoglycaemia (n=218)

Criteria	Hypoglycemia	NonHypoglycemia	Total	P-value
Maternal anemia	82	1581	1663	<0.001
Non anemic	136	971	1107	
Total	218	2552	2770	

Table-7: Clinical Features of N Hypoglycaemia (n=218)

Clinical features	No. of cases	Percentage of Total
Jitteriness & Tremor	71	32.56
Lethargy & Poor Feeding	43	19.72
Tachypnea	23	10.55
Cyanosis, Apnea	19	8.71
Convulsions	12	5.5
Weak, high pitched Cry	11	5.04
Asymptomatic	128	58.72

Table-8: Time of Development of N Hypoglycaemia (n=218)

Age		No. of Hypoglycemia (1st detected)	Percentage of Total
< 2 hours	Day - 1	27	12.38%
2-12 hours		36	16.51%
12-24 hours		56	25.68%
24-48 hours (Day-2)		36	16.51%
48-72 hours (Day-3)		63	28.90%

Table-9: Time of Development of N Hypoglycaemia (n=218)

Age	No. of Hypoglycemia	No. of Non Hypoglycemia	Total	P-value
Day-1	119	806	925	<0.001
More than Day-1	99	1746	1845	
Total	218	2552	2770	

Table-10: **Blood Glucose Values in Hypoglycaemic Babies at Different Periods of Life**

Timing of test	Asymptomatic hypoglycemia (n=128)			Symptomatic hypoglycemia (n=90)			P-value
Initial at 2/6/12/24/48 hrs	Range	Mean ± SD	No.	Range	Mean ± SD	No.	
	22-36	28.20 ± 7.9	128	12-21	17.90 ± 4.89	90	<0.0001
At 72 hours	42-67	48.32 ± 9.3	128	28-46	44.30 ± 7.30	90	=0.007

Table-11: **Initial Blood Glucose Levels in Symptomatic Hypoglycaemia (n=90)**

Initial Blood sugar levels in mg/dl	No. of symptomatic hypoglycemic	Percentage
0-10	0	0
11-20	56	62.22%
21-30	19	21.11%
31- <40	15	16.66%

Table-12: Outcome of Neonatal Hypoglycaemia (n=218)

Outcome	No	Percentage
Discharged	199	91.28%
Death	17	7.80%
Referred	2	0.92%

DISCUSSION

In the present study, the incidence of hypoglycemia in all admitted cases was 7.87%. This incidence is slightly higher than the study done by B. Kiran & Dhananjaya et al (4.2%).[4] Lubchenco & Bard in their study found that 11.4% of all nursery admissions were hypoglycemic.[5] This high incidence may be due to the fact that they have considered the threshold to be hypoglycemia as <50 mg/dl whereas in our study we have taken <40 mg/dl as the cut off value. However, the variability in incidence could also be due to different nursery practices, feeding practices and different degrees of neonatal sickness. Male babies outnumbered the females (M: F = 1.11:1). This difference might be due to the demographic trends of our country.

In our study 11.75% of preterm babies were hypoglycemic which is comparable with the study done by B. Kiran and Dhananjaya *et al*. where this incidence was 11.9%.[4] Holtrop has found the incidence of

hypoglycemia to be 14.7% in term SGA which is comparable with our study, i.e. 15.46%.[6] On the contrary, Hawdon et al, in their study found the incidence of hypoglycemia in term infants to be 0.8% and incidence of hypoglycemia in preterm infants 3.15%.[7] The variability in incidence among preterm infants may be due to the fact that there are more no of preterm babies in our country. Lubchenco & Bard found 20.3% of preterm babies to be hypoglycemic, as they have taken blood glucose level of 50 mg/dl as the cut off.[5]

Incidence of hypoglycemia in SGA is 23.10%, which is comparable with Mishra et al i.e. 26% and little lower than the study of Lubchenco & Bard i.e. 32.8%.[5, 8] This high incidence might be due to the fact they have taken 50 mg/dl as the cut off value for hypoglycemia and due to the discouragement of early feeding practices in 1970s. In their study they found that 67% of preterm SGA babies were hypoglycemic which is higher than our study (43.24%). In our study the incidence of hypoglycemia in LBW is 10.9%.

The incidence of hypoglycemia in IDM in our study is 47.61%. According to Meharban Singh (1991) the incidence of hypoglycemia is 50% in IDM and 20% in gestational diabetes.[9] The combined incidence is comparable with our study. Cordero L, Treuer SH, Landon MB in 1993 had quoted the incidence of hypoglycemia in IDM as 27%.[10]

The incidence of hypoglycemia was relatively higher in neonates when 2 independent risk factors coexist. Preterm SGA babies are more susceptible to hypoglycemia as compared to preterm alone (43.24% as opposed to 11.75%). Lubchenco & Bard (1971) have found that incidence of hypoglycemia in Preterm SGA is 67%.[5]

LBW (both preterm & term SGA) babies contributed highest with 55.05% of total hypoglycemic cases. Prematurity, birth asphyxia and SGA, as independent risk factors contributed 48.16%, 38.07%, and 14.22% of all hypoglycemia cases respectively. In the study by N. Najati and L. Saboktakin (2010). the underlying causes of hypoglycemia were prematurity (61.5%), diabetic mother(13.6%) and septicemia (9.6%).[11] Munir Akmal, Nasir Ali Shah & Ghulam Sahir in 2006, found that 46.53% of all hypoglycemic babies were low birth weight, 6.93% had birth asphyxia and 4.95% had neonatal sepsis.[12] The higher percentage of birth asphyxia babies contributing to hypoglycemia in our study might be due to the relatively higher incidence of perinatal asphyxia in our hospital.

Maternal anaemia, prolonged labour, Lower maternal age (16-20 years) and maternal fever mostly during last trimester are associated with Neonatal Hypoglycaemia in 37.61%, 24.77%, 21.10% and 11.92% cases respectively.

The fact that various Antenatal risk factors contributing to hypoglycemia indirectly by delivering more preterm, IUGR, birth asphyxiated and neonatal sepsis, have also been reported by different studies (Meharban Singh et al, 1991; NRC Robertson et al, 1999).[13,14] The study by Mishra *et al* also shows that 48.2% of all symptomatic hypoglycemia cases were associated with complicated pregnancies and deliveries.[8]

Only 41.28% of neonates with Hypoglycaemia were symptomatic in the present study which is comparable with the study by Kiran B. *et al* (2011), suggesting the incidence to be 40%.[4] Although none of the signs and symptoms of hypoglycemia are pathognomonic, Jitteriness and Tremor were the most common features in our series and have also been found by Cornblath et al and Kumari et al.[15]

Majority (94.04%) of Neonatal Hypoglycaemia were transient and rest 5.96% were persistent in which cases low blood glucose level was detected on Day-3 of life and then after, despite being treated with I.V. glucose infusion @12 mg/kg/min. Most of them were suspected of having IEM or having multiple risk factors.

Initial blood glucose values of symptomatic patients range from 12-21 mg/dl with a mean 17.90 ± 4.89 mg/dl. At 72 hours after IV glucose therapy and feeding, blood glucose value ranged from 28-46 mg/dl with a mean of 44.30 ± 7.30 mg/dl with 13 babies still having low blood glucose level after 72 hours of life. Maximum symptomatic babies have blood sugar level in the range 11-20 mg/dl. So it is concluded that with <20 mg/dl blood glucose level, there is more chance of the neonates becoming symptomatic (P value <0.0001).

In the present study, 91.28% of all hypoglycemic cases were discharged, death occurred in 7.80% of cases, while two cases were referred to other departments for further management. Some babies were discharged with some sequelae. The death rate is lower than the study by Mishra and Sharma et al.[8] This may be due to the fact that they have included only the symptomatic hypoglycemic in their study. The deaths occurred mainly due to associated morbid conditions most of them being Preterm, ELBW, Sepsis with shock and IEM.

CONCLUSION

Neonatal hypoglycemia not only can cause mortality, but also may lead to serious neurological damage in newborn period. Early detection and prompt correction of hypoglycemia before occurrence of symptoms is the most important in the first step of management, but for definite treatment, the management of underlying cause is the second important and highly essential step.

Awareness of the risk factors that predispose infants to hypoglycemia allows for screening of those at risk, so that clinically undetectable hypoglycemia can be treated promptly, thereby preventing the development of severe

or symptomatic hypoglycemia, which is associated with adverse outcome. Hence, it is recommended that regular scrutiny, screening and prompt intervention in at-risk neonates can bring a smiling future of those tiny and tender cuties. A healthy bud of today is a glowing flower of tomorrow.

LIMITATIONS

In spite of efforts being made for getting the best results in the present study, there remained some pitfalls such as:- a) This study represents only those cases of hypoglycemia which were admitted to the hospital, a tertiary care center. Thus the incidences and complication rates cannot be generalized to the population at large b) There is still no universally acceptable definition of hypoglycemia. So further research is required in this regard. c) Further it is a short-term study comprising only small no. of neonates and hence long-term studies involving large no. of cases are needed to reaffirm the substantial results.

BIBLIOGRAPHY

1. Lucas A, Morley R, Cole TJ. Adverse neurodevelopmental outcome of moderate neonatal hypoglycemia. British medical journal, 1988; 297: 1304-1308.
2. Fluge G. Clinical aspects of neonatal hypoglycemia. Actapaediatrica Scandinavica, 1974, 63: 826. WHO Bulletin OMS. Vol 75, 1997, 285 A.F. Williams.
3. Gutberlet RL, Cornblath M. Neonatal hypoglycemia revisited. Paediatrics, 1975; 58: 10-17.
4. Kiran B, Dhananjaya C.D. Prevalence and underlying Etiology of neonatal hypoglycemia, Int. Journal of Biological Medical Research, 2011; 2(4): 1110-1114.
5. Lubchencho LO, Bard H. Incidence of hypoglycemia in newborn infants classified by birth weight and gestational age. Paediatrics, 1971; 47: 831-838.
6. Holtrop PC, The frequency of hypoglycemia in full term large and small for gestational age newborns. American Journal of Perinatology, 1993; 10: 150-154.
7. Hawdon JM, Wardplatt MP, Aynsley Green A. Pattern of metabolic adaptation for preterm and term infants in the first neonatal week. Archives of disease in childhood, 1992; 67: 357-365.
8. Mishra PK, Sharma B. Hypoglycemia in newborn. A prospective study. Indian Pediatrics, 1977; 14: 129-135, 1983.
9. Singh M et al. Neurodevelopmental outcome of asymptomatic and symptomatic babies with neonatal hypoglycemia. Indian journal of medical research (B), 1991; 94: 6-10.
10. Cordero, L. and M. B. Landon (1993). "Infant of the diabetic mother." Clinics in Perinatology, 20(3): 635-648.
11. N. Najati, L. Sabotakin. Prevalence and underlying etiologies of neonatal hypoglycemia. Pakistan Journal of Biological Science, 2010; 13: 753-756.
12. Munir Akmal Lodhi, Ghulam Shabbir, Nasir Ali Shah. Risk factors associated with neonatal hypoglycemia. Professional Med journal, 2006 Dec; 13(4): 687-90.
13. Singhal PK, Singh M, Paul VK, Malhotra AK, Deorari AK, Ghorpade MD. Acontrolledstudy of sugar fortified milk feeding in prevention of neonatal hypoglycemia. Indian J Med Res., 1991; 94: 342-5.
14. NRC Robertson: Textbook of neonatology 3rd Edition, 1999; 1281-1284.
15. Kumari S. Bhargava, SK Ahmed, SH Ghosh S. Transient symptomatic hypoglycemia in the newborn. Indian Pediatr, 1971; 8: 768.