MEDICAL CHANNEL

Original Article

CLINICAL PROFILE OF HYPOGLYCEMIA IN NEONATES

** Mashal Khan, ** Kanwal Altaf Malik, *** Sana Jan*

* FCPS MCPS DCH, Department of Pediatrics and Neonatology, National Institute of Child Health, Karachi, Pakistan
** MBBS, Department of Pediatrics and Neonatology, National Institute of Child Health, Karachi, Pakistan
*** MBBS, Department of Pediatrics and Neonatology, National Institute of Child Health, Karachi, Pakistan

Received on: 16-08-2016
Accepted on: 15-09-2016

ABSTRACT

Objective: To determine the clinical manifestations of hypoglycemic neonates presenting at a tertiary care facility. **Method:** This was a cross sectional study conducted at neonatal unit, National Institute of Child Health, Karachi from 10th December 2013 to 9th December 2014. All hypoglycemic neonates of either gender and term gestation were enrolled. Detailed relevant history and clinical examination was considered i.e. Refusal to feed , jitteriness, seizures, lethargy, respiratory distress and hypothermia. Blood sample for glucose level was sent to the institutional laboratory. Blood glucose values less than 40 mg/dl (2.8mm0l/1) was considered as hypoglycemia. Data was analysed in SPSS version 17 .P value < 0.05 level as taken as significant. **Results :** Mean age , weight and gestational age of the neonates were 14.69 ± 10.23 days, 3.16 ± 0.46 kg and 3.16 ± 0.46 weeks respectively . There were 65 (59.10%) female and 45 (40.90%) male patients. Frequent clinical manifestation were refusal to feed (43%) , jitteriness (35%), respiratory distress (33%), lethargy (27%), seizures (11%) and hypothermia (11%). **Conclusion :** Refusal to feed was the commonest clinical expression in hypoglycemic neonates. It builds our threshold for management and prevention strategies towards hypoglycemic neonates with diverse clinical picture.

Key words Clinical manifestations , Hypoglycemia, Symptomatic neonates.

Med. Channel 2016; 22(3) 35-40

Correspondence Author:
DR. MASHAL KHAN
Flat No.C-3/III
Doctor's Colony, Jinnah Postgraduate Medical Centre,
Rafique-e-Shaheed Road,
Karachi-75510
Cell No. 0300-9292905
Ph: No.02135655220
E mail:
drmashal64@gmail.com

INTRODUCTION

Hypoglycemia is commonly confronted in neonatology. Neonatal hypoglycemia is not a disease in itself but a part of illness or presents the inability to cope up the extra uterine physiology .It reflects an imbalance between glucose supply versus its utilization resulting from a plenitude of immature regulatory mechanisms. Maintenance of glucose delivery to all organs is essential for the body metabolism, especially the

brain .[1] The glucose needs of the fetus are provided by the continuous trans placental glucose supply. Enzyme responsible for gluconeogenesis are present from the early pregnancy, yet the fetus makes its own glucose only in stressful situations like mother starvation .[2]

The standard definition of hypoglycemia remains under debate .[3]The incidence of hypoglycemia stands plausible due to the varied definitions.[4] A recent review suggested the operational threshold of neonatal hypoglycemia as <40 mg/dl (2.2mmol/L) in the initial 24 hours and <50mg/dL (2.8mmol/L) thereafter.[5] Cornblath et al also highlighted the idea of implementing operational threshold for hypoglycemia , rather than a single number to declare the same , as the maturity level differs among all and so does the impact of disease. [3]

The clinical spectrum of hypoglycemia remains nonspecific. They may be a part of a vast variety of disease states or can be seen in normal infants. They constitute change in the level of consciousness with a varied severity like stupor, lethargy, tremulousness, irritability ranging to coma and seizures with more profound hypoglycemia. Other signs are more variably present, including respiratory depression or actual apnea resulting in cyanosis, hypotonia, limpness, and inactivity, a high-pitched cry, poor feeding after previously feeding well and hypothermia.. The spectrum of clinical signs are due to the variable physiology (plasma flow, hematocrit, hypoxia-ischemia, etc.) and different alternate substrates.[6]Significant hypoglycemia in neonates results in neurological impairment ranging from learning disabilities , seizure disorders to cerebral palsy . It may also cause mental retardation of varied severity. [1]

Strategies to combat the variable impact of hypoglycemia should be enhanced. [7] Bedside glucose tests are used for screening high risk neonates .Moreover laboratory levels establish the diagnosis of hypoglycemia especially in asymptomatic infants .[8]

Neonatal hypoglycemia is an important aspect to be considered due to its potential complications and long term sequels. This study aim to recognize the magnitude of the potential neonates for hypoglycemia and its variable clinical impact that may be present in many other disease states , hence raising our concerns to detect as early the potential candidates ,in this context and further emphasizing in formulating strategies and research priorities to combat this cause of morbidity efficiently .

METHODS

The National institute of child Health (NICH) is a tertiary care hospital with a 100 bed neonatal care unit, one of the largest unit with advanced facilities in town . It caters a huge flow of patients all over Sindh , Balouchistan and Punjab province. This is a cross-sectional study , conducted at neonatal unit , from 10th December 2013 to 9th December 2014. Non probability consecutive sampling was done . Sample size was calculated on the basis of previous study with the confidence interval of 95 % and margin of error of 6 %[9] . A total of 110 neonates with hypoglycemia of either gender and term gestation were enrolled in the study , excluding any neonate with congenital anomaly. Symptomatic neonates were neonates with one or more of the clinical manifestations as described. Refusal to feed was labeled when feed was not taken for more than or equal to 12 hours . Jitteriness was the presence of restless bodily movement ,seizures was the presence of deviation of eye balls , bluish discoloration of mucous membranes , repetitive mouth and tongue movements or pedaling , tonic posturing of limbs , respiratory distress was respiratory rate more than 60 breaths / min , hypothermia as body temperature less than 97.7 F and lethargy was labeled with either of the following , difficult to wake up for feeding , drowsy not responding to vocal commands or sluggish movement. After approval from institutional ethical review committee, informed consent was considered from the parents/guardians. Confidentiality of the patient was assured .The following details were noted i.e. name, age, gestational age, gender , birth weight and hospital registration number. Infant's age was considered in hours and days . Detailed history and clinical examination were carried out to see for the relevant clinical manifestations as mentioned above .Blood sample was collected from a peripheral vein through aseptic technique and was sent to the institutional laboratory for blood glucose measurement . Blood glucose values less than 40mg/ dl (2.8mmol/l) was considered as hypoglycemia . All the information was compiled in a preformed proforma .Data analysis was done using SPSS version 17 .Mean ± SD was presented for neonatal age (days) , weight (kg) of the neonate and gestational age .Frequency and percentages were computed for gender , hypoglycemia , refusal to feed , jitteriness , seizures , hypothermia , lethargy and respiratory distress . Stratification was done to evaluate the effect of age , weight , gestational age and gender

on the outcome , variable and chi square test was applied . Significance level was set at 0.05 .

RESULTS

Mean age of neonates was 14.69 ±10.23 days . The minimum age being 1 day and the maximum of 28 days .

There were 61 (55.50%) neonates with the age of ? 15 days , whereas 49 (44. 50 %) were > 15 days of age .

The mean weight of the neonates was 3.16 ± 0.46 kg. Out of the total 65 (59.1 %) neonates were ? 3 kg and 45 (40.9 %) were > 3 kg .

Mean gestational age of the mother was 3.16 ± 0.46 weeks . Out of the total , 74 (67.30%) neonates had gestational age of ? 38 weeks and 36 (32.70 %) had > 38 weeks of gestation.

The study included 65 (59.10%) female patients and 45 (40.90%) male patients.

The clinical profile in hypoglycemic neonates showed refusal to feed being the most common manifestation i.e. in 47 (43 %) neonates whereas jitteriness , seizures , hypothermia , lethargy , and respiratory distress were seen in 38 (35 %) , 12 (11 %) , 12 (11%), 30 (27%) and 36 (33 %) neonates respectively (Figure 1) .

Stratification was done in regard to age , gestational age , weight and gender to see its impact in this context (Table 1-3) .

DISCUSSION

The definite frequency of hypoglycemia in high risk and general newborn nursery is unyielding due to varied definitions of hypoglycemia and different population. [10]

Rashid A . mentioned the incidence of hypoglycemia in his study as 11.5 % and Dashti et al as 15.15% .[9, 11]However, Hamid et al reported this incidence to be 38.4%[12]. Transient newborn hypoglycemia (glucose level less than 35, less than 40 and less than 45 mg/ dL) was seen in 6.4 percent, 10.3 percent and 19.3 percent of infants, respectively .[13]

The common clinical features in hypoglycemic babies were refusal to feed (48 %) ,irritability and jitteriness (38%) , tachypnea (29%) , cyanosis (19.5%) and seizures in 15 % cases .[9]

TABLE : 1

COMPARISON OF SEIZURES AND JITTERINESS WITH OTHER VARIABLES
N=110

Variables		Seizures			Jitteriness		
		Yes	No	p-value	Yes	No	p-value
Age	≤15 n=61	7 (11.5%)	54 (88.5%)	0.832	33 (54.1%)	28 (45.9%)	0.001
	>15 n=49	5 (10.2%)	44 (89.8%)		5 (10.2%)	44 (89.8%)	
Weight	≤3 n=65	7 (10.8%)	58 (89.2%)	0.955	33 (50.8%)	32 (49.2%)	0.001
	>3 n=45	5 (11.1%)	40 (88.9%)		5 (11.1%)	40 (88.9%)	
Gestational Age	≤38 n=74	9 (12.2%)	65 (87.8%)	0.546	25 (33.8%)	49 (66.2%)	0.810
	>38 n=36	3 (8.3%)	33 (91.7%)		13 (36.1%)	23 (63.9%)	
Gender	Male 45	12 (26.7%)	33 (73.3%)	0.001	17 (37.8%)	28 (62.2%)	0.s553
	Female 65	0 (0.0%)	65 (100%)		21 (32.3%)	44 (67.7%)	

TABLE : 2

COMPARISON OF RESPIRATORY DISTRESS AND REFUSAL TO FEED WITH OTHER VARIABLES
N=110

Variables		Respiratory Distress			Refusal to Feed		
		Yes	No	p-value	Yes	No	p-value
Age	=15 n=61	28 (45.9%)	33 (54.1%)	0.001	34 (55.7%)	27 (44.3%)	0.002
	>15 n=49	8 (16.3%)	41 (83.7%)		13 (26.5%)	36 (73.5%)	
Weight	=3 n=65	28 (43.1%)	37 (56.9%)	0.005	34 (52.3%)	31 (47.7%)	0.015
	>3 n=45	8 (17.8%)	37 (82.2%)		13 (28.9%)	32 (71.1%)	
Gestational Age	=38 n=74	23 (31.1%)	51 (68.9%)	0.598	34 (45.9%)	40 (54.1%)	0.328
	>38 n=36	13 (36.1%)	23 (63.9%)		13 (36.1%)	23 (63.9%)	
Gender	Male 45	20 (44.4%)	25 (55.6%)	0.029	25 (55.6%)	20 (44.4%)	0.024
	Female 65	16 (24.6%)	49 (75.4%)		22 (33.8%)	43 (66.2%)	

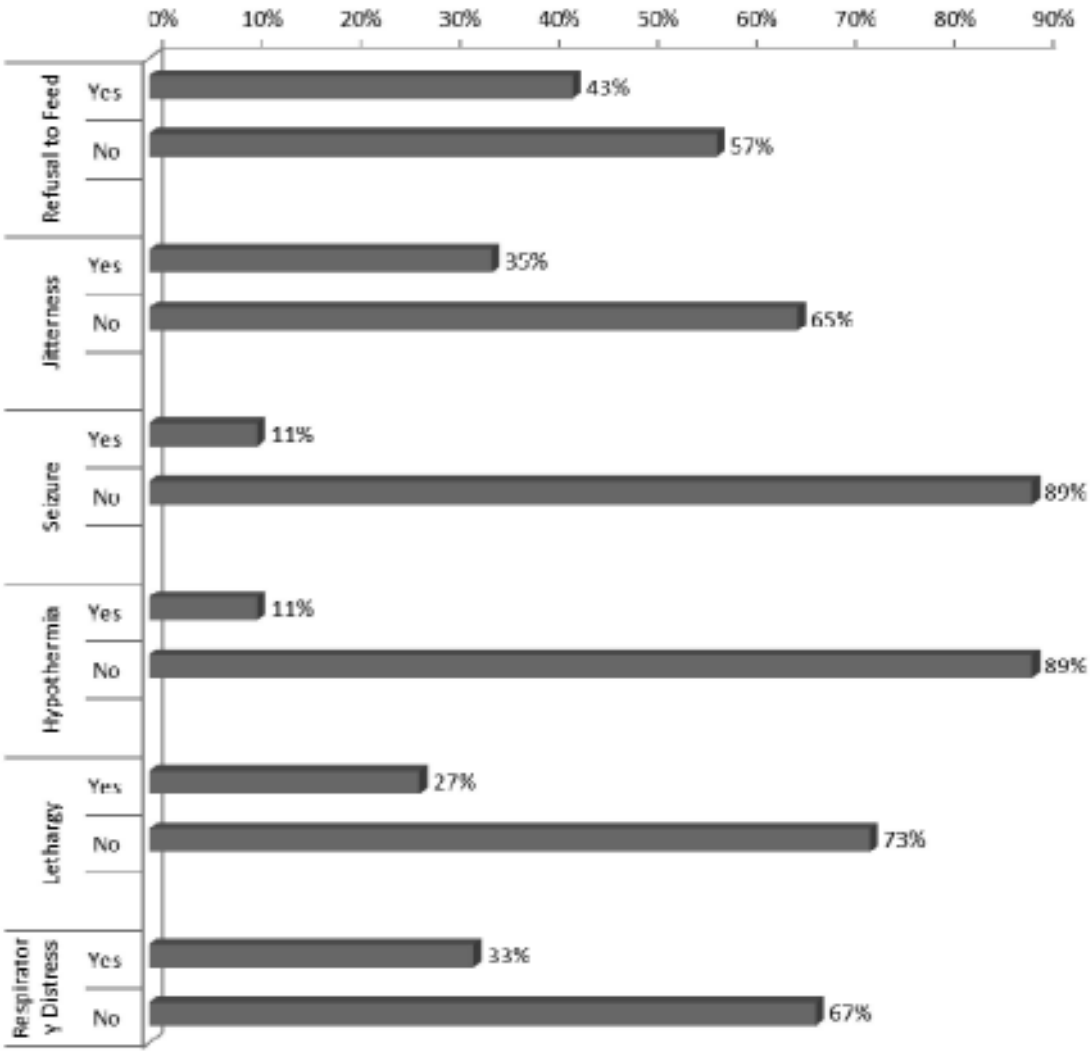
TABLE : 3

COMPARISON OF HYPOTHERMIA AND LETHARGIC WITH OTHER VARIABLES
N=110

Variables		Hypothermia			Lethargic		
		Yes	No	p-value	Yes	No	p-value
Age	=15 n=61	9 (14.8%)	52 (85.2%)	0.149	18 (29.5%)	43 (70.5%)	0.557
	>15 n=49	3 (6.1%)	46 (93.9%)		12 (24.5%)	37 (75.5%)	
Weight	=3 n=65	9 (13.8%)	56 (86.2%)	0.235	18 (27.7%)	47 (72.3%)	0.905
	>3 n=45	3 (6.7%)	42 (93.3%)		12 (26.7%)	33 (73.3%)	
Gestational Age	=38 n=74	10 (13.5%)	64 (86.5%)	0.209	17 (23.0%)	57 (77.0%)	0.147
	>38 n=36	2 (5.6%)	34 (94.4%)		13 (36.1%)	23 (63.9%)	
Gender	Male 45	12 (26.7%)	33 (73.3%)	0.001	24 (53.3%)	21 (46.7%)	0.001
	Female 65	0 (0.0%)	65 (100%)		6 (9.2%)	59 (90.8%)	

FIGURE : 1

FREQUENCY OF VARIABLE CLINICAL MANIFESTATIONS IN HYPOGLYCEMIA



In another study, out of 150 symptomatic neonates , 44 (29.3 %) , were found to be hypoglycemic, feeding difficulty was the most frequent manifestation of hypoglycemia i.e. 32 (72.7%) cases followed by jitteriness in 28 (62.7%) cases , seizures 16 (37.3 %), respiratory distress 15 (34 %) , lethargy 13 (30 %) and hypothermia in 11 (26.7%) subjects. [14]

In our study , clinical spectrum included refusal to feed in 47 (43 %) , jitteriness in 38 (35 %) , seizures in 12 (11%) , hypothermia in 12 (11 %) ,lethargy in 30 (27 %) and respiratory distress in 36 (33 %) subjects .

One large prospective study established that persistent hypoglycemia had no association to worse neurodevelopmental sequel in preterm infants. But hyperinsulinism associated hypoglycemia and genetic causes, resulted in brain damage and related consequences .[15]

Based on epidemiology there is a vague cut off between hypoglycemia and normoglycemia also establishes that hypoglycemia shows a range of biologic abnormalities , from mild to severe [3] .Various authors suggest the definition of hypoglycemia in quantity specifically between 30 and 50 mg/ dl (1.7 – 2.8 mmol/

l) adjusted to varying postnatal age .[16-22]

High risk neonates should be monitered routinely for blood glucose level with frequency and duration according to the distinct risk factors of the individuals.[23] According to the Canadian Paediatric Society guidelines, a significantly low concentration of glucose in plasma should be reliably established and treated to restore glucose values to a normal physiologic range. [24]

CONCLUSION

We observed the varied clinical manifestation in hypoglycemic neonates . A high index of suspicion with constellation of signs and symptoms will help us prevent this morbidity and modifies our management strategies and research priorities.

REFERENCES

1. Rozance PJ, Hay Jr WW. Describing hypoglycemia—definition or operational threshold? Early human development. 2010;86(5):275-280.
2. Gustafsson J. Neonatal energy substrate production. Indian J Med Res. 2009;130(5):618-623.
3. Cornblath M, Hawdon JM, Williams AF, Aynsley-Green A, Ward-Platt MP, Schwartz R, et al. Controversies regarding definition of neonatal hypoglycemia: suggested operational thresholds. Pediatrics. 2000;105(5):1141-1145.
4. Sexson WR. Incidence of neonatal hypoglycemia: a matter of definition. The Journal of pediatrics. 1984;105(1):149-150.
5. Chan S. Neonatal hypoglycemia. UpToDate version. 2011;16.
6. Hawdon J, Platt MW, Aynsley-Green A. Patterns of metabolic adaptation for preterm and term infants in the first neonatal week. Archives of disease in childhood. 1992;67(4):357-365.
7. Platt MW, Deshpande S, editors. Metabolic adaptation at birth. Seminars in Fetal and Neonatal Medicine; 2005: Elsevier.
8. Hawdon JM, Platt MPW, Aynsley-Green A. Neonatal hypoglycaemia—Blood glucose monitoring and baby feeding. Midwifery. 1993;9(1):3-6.
9. Rashid A, Zaheer A, Khan Hi Neonatal Hypoglycemia: Frequency and Clinical Manifestations in a Tertiary Care Centre. Pakistan Paediatric. 2010:80-84.
10. Lubchenco LO, Bard H. Incidence of hypoglycemia in newborn infants classified by birth weight and gestational age. Pediatrics. 1971;47(5):831-838.
11. Dashti N, Einollahi N, Abbasi S. Neonatal hypoglycemia: Prevalence and clinical manifestations in Tehran Children's Hospital. Pakistan Journal of Medical Sciences. 2007;23(3):340-343.
12. Hamid M, Chishti A, Maqbool S. Clinical utility and accuracy of a blood glucose meter for the detection of neonatal hypoglycemia. Journal of the College of Physicians and Surgeons—Pakistan: JCPSP. 2004;14(4):225-228.
13. Kaiser JR, Bai S, Gibson N, Holland G, Lin TM, Swearingen CJ, et al. Association between transient newborn hypoglycemia and fourth-grade achievement test proficiency: a population-based study. JAMA pediatrics. 2015;169(10):913-921.
14. Khan I, Muhammad T, Khan MQ. Frequency and clinical characteristics of symptomatic hypoglycemia in neonates. Gomal Journal of Medical Sciences. 2010;8(2):117-120.
15. Rozance PJ. Update on neonatal hypoglycemia. Current opinion in endocrinology, diabetes, and obesity. 2014;21(1):45-50.
16. Srinivasan G, Pildes R, Cattamanchi G, Voora S, Lilien L. Plasma glucose values in normal neonates: a new look. The Journal of pediatrics. 1986;109(1):114-117.
17. Heck LJ, Erenberg A. Serum glucose levels in term neonates during the first 48 hours of life. The Journal of pediatrics. 1987;110(1):119-122.
18. Kalhan S, Peter-Wohl S. Hypoglycemia: what is it for the neonate? American journal of perinatology. 1999;17(1):11-18.
19. Cole MD, Peevy K. Hypoglycemia in normal neonates appropriate for gestational age. Journal of perinatology: official journal of the California Perinatal Association. 1993;14(2):118-120.
20. Stanley CA, Baker L. The causes of neonatal hypoglycemia. New England Journal of Medicine. 1999;340(15):1200-1201.
21. Schwartz RP. Neonatal hypoglycemia: how low is too low? The Journal of pediatrics. 1997;131(2):171.
22. Alkalay A, Klein A, Nagel R, Sola A. Neonatal non-persistent hypoglycemia. Neonatal Intensive Care. 2001;14(2):25-34.
23. Eidelman AI. Hypoglycemia and the breastfed neonate. Pediatric Clinics of North America. 2001;48(2):377-387.
24. Adamkin DH. Postnatal glucose homeostasis in late-preterm and term infants. Pediatrics. 2011;127(3):575-579.

Authors contribution:
* Conceived, design, statistical analysis,editing of manuscript, ** Data collection, manuscript writing and editing *** Data collection, preparation and review

Conflict of interest: Non conflict of interesta