THE STUDY OF VISUAL EVOKED POTENTIAL IN INFANTS WITH NEONATAL HYPOGLYCEMIA

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Abstract

Background-Hypoglycemia is one of the most common and preventable metabolic disorder affecting neonates. It can lead to irreparable brain injury, repeated seizure activity and severe comorbidities in children. Multiple studies have reported MRI brain findings of parieto-occipital diffusion restriction after symptomatic neonatal hypoglycaemia .In this study it is hypothesised that there would be a correlation between abnormal visual evoked potential and occipital injury after neonatal hypoglycaemia because it is known that occipital injury can occur after neonatal hypoglycaemia.

Aim- To determine the changes in visual evoked potential in infants with neonatal hypoglycaemia ,its correlation with MRI brain findings and numerous variables and risk factors of neonatal hypoglycaemia.

Methodology-This is a cross-sectional, observational and descriptive study carried out on 50 neonates who had hypoglycaemia and then followed up at 3 months of age for VEP study. Detailed history and various risk factor's where recorded. MRI brain was also done in these neonates. Data was collected and analysed using SPSS. Association between two categorical variables was analysed using chi square test $p<0.05$ was taken as statistically significant value at 95 %confidence interval.

Results-In this study from a total of 50 neonates, 32 were males and 18 were females. Patients with risk factors of IUGR and sepsis, 27.3% respectively showed VEP with P100 latency prolonged and 13.6% of neonates with perinatal hypoxia was significantly more.In this study. A total 86.3% of the infants who had symptomatic neonatal hypoglycemia showed VEP with P100 latency prolonged. Those infants with MRI brain findings of diffusion restriction in parieto-occipital region showed VEP P100 latency prolonged which is significant with P value of 0.001.

Conclusion- In this study, it was observed that neonates who had increased episodes of hypoglycemia showed VEP with P100 latency prolonged than those with normal VEP. The infants with symptomatic hypoglycemia were more among the infants with VEP P100 latency prolonged than asymptomatic neonates .In this study it was found that there is strong correlation of MRI brain findings of occipital lobe injury and abnormal VEPs showing P100 latency prolonged and thus visual cortical dysfunction.

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1. Introduction

It is known that hypoglycaemia in neonates can have neurologic consequences that might last either temporarily or permanently. Neonatal seizures and neurophysiological abnormalities are examples of some of the short-term impacts, long term effects includes disability visual impairment, and epilepsy.[1,2] In a healthy new born infant, all of the glucose in the foetal bloodstream comes from the mother via the placenta. This is true even in the absence of any stress. As a result, the glucose concentration in the foetal blood normally mirrors the glucose levels in the mother blood. Because of the abrupt halt in glucose transmission from the mother to the foetus that occurs during delivery, there is an immediate requirement to mobilise glucose from the body's own stores.[3] In a study done at the Institute of Maternal and Child Health (IMCH) in Kozhikode, India, the incidence of neonatal hypoglycaemia was 41 out of every 1000 live births. Hypoglycaemia is common among neonates with history of perinatal hypoxia, infants of diabetic mothers, low birth weight for their gestational age and have intrauterine growth restriction (IUGR)[4] ·Some neonates with hypoglycaemia are asymptomatic , while others do display symptoms and are at risk for developing lasting brain damage . Infants who have experienced severe, prolonged, or recurring symptomatic hypoglycaemia are more likely to develop neurologic morbidity[5]. Individuals who experienced protracted neonatal hypoglycaemia have only been the subject of a small number of research, but those studies have documented neurological abnormalities in these children[6].Since the first case report in 1994,[6] other studies have confirmed the findings of parieto-occipital white matter abnormalities after symptomatic neonatal hypoglycaemia .These findings were found in neonates with hypoglycaemia that occurred during the first week of life. [7] Studies conducted more recently on diffusion-weighted imaging (DWI) have found evidence of diffusion restriction mostly in the occipital region. [8, 9] .In a separate investigation, it was discovered that half of term infants, but none of the preterm infants, had restricted diffusion in the occipital lobes. Additionally, when visual evoked potential was performed on the same children, 55 percent of them showed inadequate or nonexistent cortical response. [10] In this study it is hypothesised that there would be a correlation between abnormal visual evoked potential and occipital injury after neonatal hypoglycemia because it is known that occipital injury can occur after neonatal hypoglycaemia. The purpose of this study is to determine changes in visual evoked potentials at 3 months of age who had hypoglycaemia in the neonatal period and its association with numerous variables and risk factors of neonatal hypoglycaemia.

AIM - To determine the changes in visual evoked potential in infants with neonatal hypoglycaemia.
Objectives- 1. To study the changes in Visual evoked potentials in infants with neonatal hypoglycaemia at 3 months of age.
2. To study the various patterns of brain injury in MRI and its correlation with Visual Evoked Potential (VEP) .
3. To study number of episodes of hypoglycemia and the changes observed in VEP.

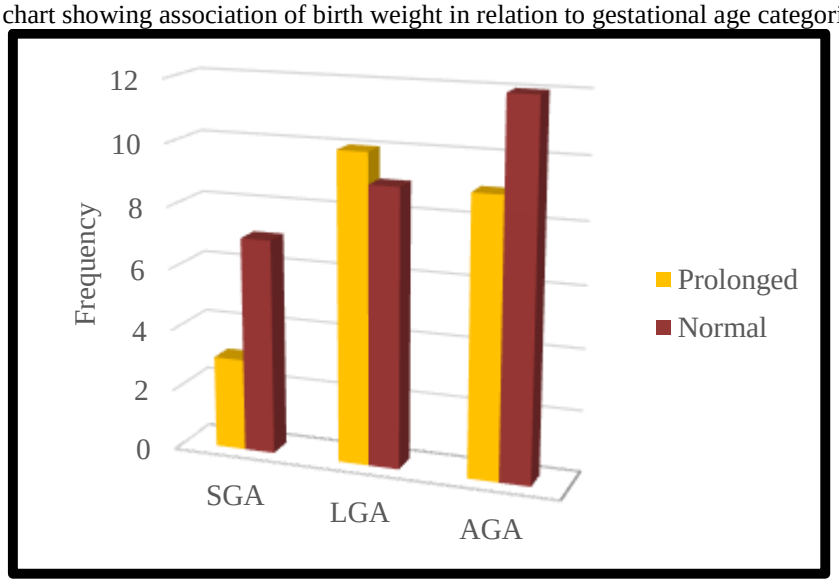
2. Methodology

This cross sectional observational and descriptive study was conducted in a tertiary care hospital over a period of 2 years. The Institutes Ethics Committee clearance was obtained before starting the study. Term newborns with neonatal hypoglycemia(blood sugar level <45 mg/dl) admitted to Neonatal intensive care unit and then followed up at 3 months of age fulfilling the inclusion and exclusion criteria were enrolled in the study. A written informed consent was taken from the parents before enrollment of neonates in the study. Blood Glucose estimation was done initially by glucose strip method using a Glucometer as well as by whole blood sugar levels by oxidase method using auto analyzer. Newborns with whole blood sugar levels less than 45 mg/dl in both the samples were taken up for study. These neonates were subjected to detailed history taking, thorough clinical examination and investigations and details of it were documented in a structured clinical proforma. Various associated maternal risk factors like gestational diabetes mellitus, pregnancy induced hypertension and, Intrauterine growth restriction IUGR , sepsis , birth asphyxia (APGAR score <7) were recorded. These neonates were managed and treated as per standard NICU protocol of the institute. MRI brain of all neonates was done by 5 to 6 days of life (as per NICU protocol) and the findings were documented. The enrolled neonates were then followed up in the high risk OPD , at 3 months of age for Visual evoked potentials study P 100 latency was analyzed and interpreted as normal / prolonged or absent.Data was collected and analysed using SPSS (Statistical Package for Social Sciences). Association between two categorical variables was analysed using chi square test $p<0.05$ was taken as statistically significant value at 95 %confidence interval. Student t test (Two tailed) will be used to test the significance of mean of two group with $P<0.05$ as statistically significant value at 95% confidence interval.

3. Results

In this study from a total of 50 neonates, 32 were males and 18 were females. A total of 14.3% of SGA, 57.1% of LGA and 28.6% of AGA showed MRI with diffusion restriction in the parieto-occipital region. In neonates with risk factors of IUGR and sepsis, 27.3% respectively showed VEP with P100 latency prolonged and 13.6% of neonates with perinatal hypoxia were significantly more with P value of 0.044.Those neonates with additional comorbidity of perinatal hypoxic injury had significantly abnormal VEP findings compared to other risk factors.In this study, 42% of the neonates presented with asymptomatic hypoglycemia and 58% presented with symptomatic hypoglycemia from which 32% had seizures, 16% had lethargy and 10% had jitteriness .The proportion of neonates with MRI brain findings of diffuse restriction in parieto-occipital region was significantly high among those with neonatal seizures (88.9%). In this study, 86.3% of the infants who had symptomatic neonatal hypoglycemia showed VEP with P100 latency prolonged which is highly significant with P value of 0.004.Those infants with symptomatic hypoglycemic were more affected by NHBI compared to asymptomatic infants.In this study, it was observed that those with VEP -P100 latency prolonged were found to have increased episodes of hypoglycemia than those with normal VEP. The difference was statistically significant with P value of 0.005.Those infants with increased episodes of hypoglycemia were more affected than those with lesser episodes.In this study, infants with VEP showing prolonged P100 latency, 59.1% had diffusion restriction in the parieto-occipital region and 40.9% had both diffusion restriction in the parieto-occipital region and findings of HIE. Those infants with MRI brain findings of NHBI showed VEP P100 latency prolonged which is significant with P value of 0.001.There is a strong correlation of MRI brain findings of occipital lobe injury and abnormal VEPs and is directly proportional.

Chart 1: Bar chart showing association of birth weight in relation to gestational age categories with VEP



Among the participants with prolonged P100 latency in VEP, 13.6% were SGA 45.5% were LGA and 40.9% were AGA .The distribution of birth weight in relation to gestational age categories was similar across different VEP categories with P value of 0.501

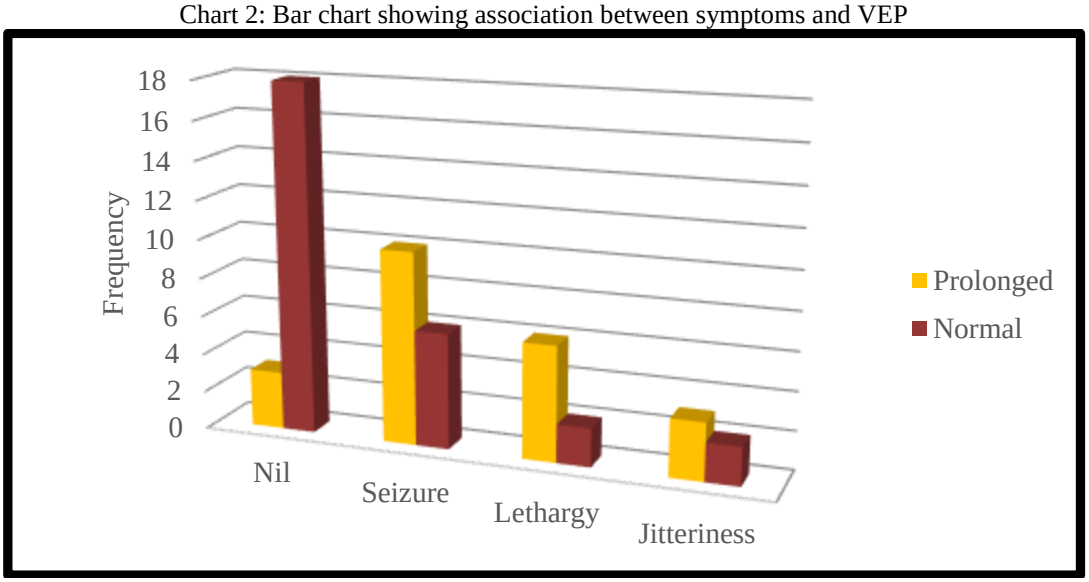
Table 1: Association between additional risk factors categories and VEP findings

Additionall risk factors categories	Prolonged P100 latency		Normal		X^2	P value
	N	%	N	%		
IUGR	6	27.3	4	14.3	1.299	0.254
Sepsis	6	27.3	4	14.3	1.299	0.254

Perinatal hypoxia	3	13.6	0	0	4.06	0.044

In this study neonates with risk factors of IUGR and sepsis 27.3% respectively showed VEP with P 100 latency prolonged, whereas all those neonates with perinatal hypoxia 13.6 % was significantly more with VEP P100 latency prolonged than those with normal VEP with P value of 0.044.

Chart 2: Bar chart showing association between symptoms and VEP



In this study a total of 86.3% had symptomatic neonatal hypoglycaemia with VEP showing P 100 latency prolonged than those who had asymptomatic hypoglycaemia was 35.6 %. The patients with symptomatic hypoglycaemia was more among the infants with VEP P 100 latency prolonged than asymptomatic neonates with P value of 0.004.

Table 2: Association between number of episodes of hypoglycaemia and VEP findings

Number of episodes of hypoglycaemia	P100 latency delayed		Normal		X^2	P value
	N	%	N	%		
1	0	0	4	14.3	14.96	0.005
2	4	18.2	16	57.1		
3	11	50	6	21.4		
4	3	13.6	1	3.6		
5	4	18.2	1	3.6		

In this study it was observed that those with VEP ; P 100 latency prolonged were found to have increased episodes of hypoglycaemia than those with normal VEP. The difference was statistically significant with P value of 0.005.

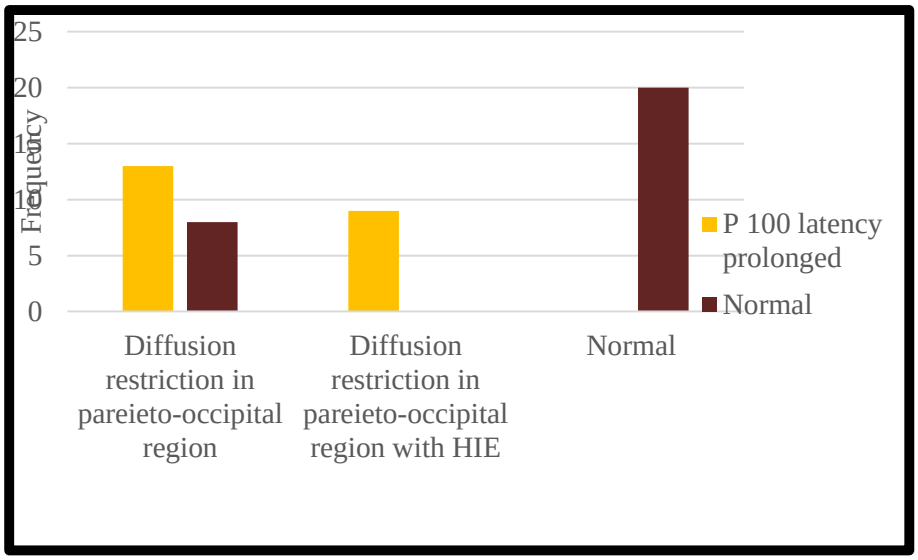
Table 3: Association between VEP findings and MRI brain findings.

MRI findings	P100 latency prolonged		Normal		X^2	P value
	N	%	N	%		

Diffusion restriction in parieto-occipital region	13	59.1	8	28.6	29.90	0.001
Diffusion restriction in parieto-occipital region with HIE	9	40.9	0	0		
Normal	0	0	20	71.4		

In this study infants with VEP showing prolonged P100 latency 59.1% had Diffusion restriction in parieto-occipital region and 40.9% had both Diffusion restriction in parieto-occipital region and findings of HIE in MRI while those with normal VEP, 28.6% had Diffusion restriction in parieto-occipital region. The pattern of MRI findings were not similar between those with prolonged VEP and normal VEP with P value of 0.001. Those with prolonged VEP had more abnormal MRI brain findings.

Chart 3: Bar chart showing association between VEP and MRI findings.



4. Discussion

This cross-sectional, observational and descriptive study was conducted in the Neonatal Intensive Care Unit and of a tertiary care center , Patients were followed up at 3 months of age at a high risk OPD to study the visual evoked potential in infants with neonatal hypoglycemia. In this study it was found that among the 50 term neonates enrolled, 64% were male and 36% were female. Hence it has been found that the incidence of neonatal hypoglycaemia is found to be higher in males which is similar to a recent 2022 study done by Gurbuz G .et.al.[11] who included a total of 70 cases out of which twenty-eight (40%) were girls and 42 (60%) were boys. In this study, infants with prolonged P100 latency in VEP, 13.6% were SGA, 45.5% were LGA and 40.9% were AGA. The distribution of birth weight in relation to gestational age categories was similar across different VEP categories. Kumar.et.al.[12] found a higher incidence of hypoglycaemia in SGA neonates (55.4%), which was attributed to the increase in the proportion of SGA in India and standardized blood glucose level monitoring as the reasons for this high incidence. Pillai.et.al.[13] showed that 70% of the babies were of AGA, while 3.2% were LGA and 26.8% were SGA. The most common risk factors included in this study were sepsis and IUGR followed by perinatal hypoxia. In this study, 27.3% of the neonates with risk factors of IUGR and sepsis respectively, showed VEP with P100 latency prolonged, whereas all those neonates with perinatal hypoxia 13.6 % had significantly more VEP P100 latency with significant P value of 0.044. In this study, it was found that neonates with IUGR of 38%, sepsis of 33.3 % had MRI findings

of diffusion restriction in the pareito-occipital region. The neonates who had perinatal hypoxic insult of 33.3%, the MRI showed diffusion restriction in the parieto-occipital region with findings of hypoxic ischemic encephalopathy with highly significant P value of 0.001. Similar findings are found in a study performed by Tam EW.et.al.[14] who observed that 13 children had secondary hypoglycaemia which was associated with other illnesses including asphyxia, intracranial haemorrhage, sepsis and congenital heart diseases. Another recently published 2022 study by Uyur Yalçın E.et.al.[15] reported sepsis in 9 patients out of 42, a total of 9 patients manifested microcephaly and 7 patients manifested cerebral palsy. In this study, a total of 86.3% had symptomatic neonatal hypoglycaemia with VEP showing P100 latency prolonged than those who had asymptomatic hypoglycaemia which was 35.6 %. The patients with symptomatic hypoglycaemia were more among the infants with VEP P100 latency which is statistically significant with P value 0.004 In this study, neonates with symptomatic hypoglycaemia, 33.3% with seizures, 33.3% with lethargy, 14.3% with jitteriness and 19% of asymptomatic patients, showed MRI with diffuse restriction in the parieto-occipital region. Among those who showed MRI findings of diffuse restriction in parieto-occipital region, 88.9% had neonatal seizures. The distribution of symptomatic neonatal hypoglycaemia was found to be highly significant among those with MRI findings of neonatal hypoglycaemic brain injury with P value of 0.001. The above results are in agreement with Kinnala.et.al.[16] who reported that the relative risk of the hypoglycaemic child compared with non-hypoglycaemic child to have any abnormality detected in the brain. Spar.et.al.[17] presented the MRI findings of 1 infant at the age of 19 days after 15 hours of severe hypoglycaemia. They found progressive parenchymal loss and predominantly occipital involvement. It was observed that those with increased episodes of hypoglycaemia had VEP P100 latency prolonged. The difference was statistically significant with P value of 0.05. Kinnala.et.al.[16] compared the distribution of the low serum glucose concentrations with the MRI and the Ultrasound (USG) imaging findings out of which 42% of the infants with two or more episodes of low serum glucose concentrations had abnormalities in the MRI or in the USG findings and they did not differ from the new-borns with only one hypoglycaemic episode. In this study, infants with VEP showing prolonged P100 latency, 59.1% had diffusion restriction in the parieto-occipital region and 40.9% had both diffusion restriction in the parieto-occipital region and findings of HIE. This infers that those neonates with MRI findings of neonatal hypoglycaemic brain injury showed VEP with P100 latency prolonged which is highly significant with P value of 0.001. Tam.et.al.[14] performed VEP studies within 1 week after the onset of hypoglycaemia for 20 out of the 25 neonates in the study cohort. 11(55%) of the 20 neonates showed poor or absent cortical responses in VEP testing. Significant association between VEP results and occipital diffusion restriction was found.

5. Conclusions

In this study, it was observed that neonates who had increased episodes of hypoglycemia showed VEP with P100 latency prolonged than those with normal VEP. Those infants with increased episodes of hypoglycemia were more affected than those with lesser episodes.The infants with symptomatic hypoglycemia (86.3%) was more among the infants with VEP P100 latency prolonged than asymptomatic neonates which is statistically significant with P value of 0.004. Those infants with symptomatic hypoglycemic were more affected by NHBI compared to asymptomatic infants.Thus in this study it was found that there is strong correlation of MRI brain findings of occipital lobe injury and abnormal VEPs showing P100 latency(the wave form measured using scalp occipital electrodes) and thus visual cortical dysfunction.

6. References

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