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AN OBSERVATION OF CARDIOVASCULAR DYSFUNCTION IN NEONATES WITH BIRTH ASPHYXIA

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Abstract:

Background

Asphyxia is an important cause of static developmental and neurologic handicaps both in Term and Preterm infants. The most frequent abnormalities involving kidneys (50%) followed by central nervous system (CNS) (28%), cardiovascular system (CVS) (25%), and pulmonary system (23%). The incidence of cardiac dysfunction in perinatal asphyxia can be identified by the clinical presentations. Apart from that echocardiogram (ECHO), electrocardiography (ECG) and determination of cardiac enzyme levels were considered as useful diagnostic tools to detect myocardial involvement. this study aimed to observe the changes in echocardiography, ECG, and cardiac enzymes as well as to assess their correlation with different stages of hypoxic-ischemic encephalopathy (HIE) and outcome.

Method

This is a prospective, observational cross-sectional study is carried out at Special Newborn Care Unit (SNCU) of tertiary care center of Uttar Pradesh, India. Duration of this study was from July 2021 to October 2022. We enrolling study population as per inclusion and exclusion criteria. Investigation was carried out and data calculation was done by using appropriate test of Significance

Results:

Out of all neonates, 84.6% neonates showed abnormal ECG in the form of flat or inverted T waves on 1 or more limb leads or ST depression/elevation in chest leads or an abnormal q wave. Most number of newborns (32.5%) had Grade 3 ECG changes. Echo was abnormal in 44 babies and all required ionotropic support for 1-5 days. Among the newborns, a significant proportion (70.7%) showed elevated creatinine kinase-MB (CK-MB) levels exceeding 92.6 IU/L. Notably, the majority of patients fell within the range of 150 to 250 IU/L.

Conclusion:

Cardiovascular dysfunction was prevalent among neonates following asphyxia, and those with compromised cardiac function had poorer outcomes. Early screening and robust cardiovascular support may enhance outcomes for neonates affected by asphyxia.

Key words:

Birth asphyxia, neonate, cardiovascular dysfunction, echocardiography

Introduction

Perinatal hypoxia is one of the leading causes of mortality and morbidity in developing countries like India, and even in developed countries. Asphyxia is an important cause of static developmental and neurologic handicaps both in Term and Preterm infants. The way an asphyxiated baby is managed, determines the mortality and quality of life among survivors. The survivors have increased risk of epilepsy, mental retardation, neonatal encephalopathy, deafness, visual impairment and disorders of learning and behavior in later childhood.[1] The focus in perinatal asphyxia is mostly on the brain, due to hypoxic-ischemic encephalopathy causing mortality or morbidity with sequelae in many cases. Other organ systems also suffer the consequences of hypoxic-ischemic insult but are often overlooked. Target organs of perinatal asphyxia are the brain, heart, lungs, kidneys, gut, and bone marrow. The most frequent abnormalities involving kidneys (50%) followed by CNS (28%), CVS (25%), and pulmonary system (23%). Thus, there is evidence of multiorgan system dysfunction in the immediate neonatal period.[2]The incidence of clinical cardiac dysfunction in perinatal asphyxia varies from 24–60%.[3] The heart failure was the main

recognized manifestation of myocardial dysfunction after perinatal asphyxia.[4] A murmur suggestive of atrioventricular value insufficiency, electrocardiographic abnormalities characteristic of myocardial ischemia or both were found in 29% of the infants who were suspected to have cardiac involvement.[5] Other recognized complications include cardiogenic shock and hypotension, functional tricuspid incompetence secondary to acute cardiac dilation, arrhythmia, The incidence of cardiac dysfunction in perinatal asphyxia can be identified by the clinical presentations. Apart from that echocardiogram, ECG and determination of cardiac enzyme levels were considered as useful diagnostic tools to detect myocardial involvement. Therefore, the present study was done with the objective to assess the usefulness of echocardiography, ECG, and cardiac enzymes in evaluating myocardial damage in perinatal asphyxia neonates and to assess their correlation with different stages of HIE and outcome.

MATERIALS AND METHOD:

Study design

This was a prospective observational cross sectional, hospital-based study.

Site of study: This study is carried out at SNCU of a tertiary care center.

Duration of study: This study was done from July 2021 to October 2022.

Inclusion criteria: Term neonates having any one of following feature included for the study.

1. Apgar score of ≤7 at 5 min
2. Umbilical cord arterial pH of <7.2 at birth
3. Required more than 1 min of positive pressure ventilation before sustained respiration or need for mechanical ventilation
4. Signs of neurologic dysfunction like seizure, encephalopathy, tone abnormalities
5. Clinical feature of multi-organ dysfunction

Exclusion criteria:

1. Neonates born before 37 weeks of gestation,
2. Born with major congenital anomalies
3. Having early-onset sepsis
4. Severe cyanosis present at birth
5. Parents not giving consent

Data collection:

In the study, all newborn babies who met both the inclusion and exclusion criteria were enrolled. Written consent was obtained from the parents, and a detailed history was recorded along with a clinical examination at the time of admission to the SNCU. The neonatal clinical course was then followed until the baby was discharged. Newborns with asphyxia are categorized into different

stages according to Sarnat and Sarnat staging.[6] All neonates were managed as per Neonatal Resuscitation Program (NRP) guidelines and supportive management given in the form of oxygen via hood, continuous positive airway pressure (CPAP) and mechanical ventilation as needed depending on the clinical condition, IV fluids and IV antibiotics were given to babies who required respiratory support. IV Inotropes and anticonvulsants were given as per need.

Blood samples for CK-MB were taken at 8 hours of life by taking 1-2ml of blood and analyzed by quantitative determination using semi auto-analyzer. A 12 lead ECG was taken within 24 hours of life and was graded as per Jedeikin et al into four grades.[7]

•Grade 1: Flat or inverted T waves on 1 or 2 limb leads except AVR

• Grade 2: Flat or inverted T-waves in 3 or more leads except AVR

• Grade 3: Flat or inverted T-waves in 3 or more leads and either ST depression or elevation >2 mm in at least two chest leads or >1 mm in at least two standard leads, or a Q-wave abnormality of duration >0.02 s or amplitude >25% of R wave in one anterior or three related chest leads.

• Grade 4: Presence of classical segmental infarction with abnormal Q-wave and markedly elevated ST segment or complete left bundle branch block.

CK-MB isoenzyme levels were estimated at 8 h of life in all neonates. A value of more than 92.6 U/L at 8 h was taken as high. An ECHO was also carried out after 24 h of life.[8]

Statistical analysis:

The data were compiled and analyzed using descriptive statistics using Chi-square test. The P< 0.05 was considered to be statistically significant.

RESULTS:

Total 123 newborn babies were enrolled for the study, out of which 18 were expired. 78 were male baby and 45 were female. 67 babies were delivered by vaginal route and 56 were delivered by caesarian section. Most newborn babies (69) from having birth weight between from 2.5 to 3 kg as shown in Table no.1.

Table no 1: Demographic profile of study population.

S.N.	Demographic profiles of newborn		Number of newborn n= 123	Percentage %
1.	Sex	Male	78	63.4
		Female	45	36.6
2.	Mode of delivery	Normal vaginal delivery	67	54.5
		Caesarian section	56	45.5
3.	Birth weight	2- 2.5 kg	21	17.1
		2.5 – 3 kg	69	56.1
		3- 3.5 kg	24	19.6
		>3.5 kg	9	7.3

Only 37.4% of the neonates were born through meconium-stained liquor while in rest it was clear. Among the newborns who needed positive pressure ventilation using bag and mask, a significant proportion also required intubation. About 43 (34.9%) of the neonates had an APGAR score less than 3 and 43.9 % having score between 3 to 5 at five minutes of life. Shock was present in 43.9 % of babies out of 123. 64.2% % had a cord blood pH between 7.0 and 7.2 and pH of <7 was noted in 35.8 % of babies.

As per Sarnat and Sarnat staging, 30 % of newborns belonged to HIE stage 1, 40.7% belongs to HIE stage 2 and about 23.3% neonates were severely asphyxiated with HIE stage 3. Most neonate 51.2% stayed in hospital between 7 to 14 days. The survival rate was 85.4% in our study.

Table no 2: Clinical characteristics of the study population

S.N.	**Clinical Characteristics of newborn**		**Number of newborns = 123**	**Percentage %**
1.	Color of liquor	clear	77	62.6
		meconium stained	46	37.4
2.	Apgar score at 5 min	< 3	43	34.9
		3-5	54	43.9
		5-7	26	21.2
3.	Positive pressure ventilation	Only Bag & mask ventilation	57	57.7
		Intubation required	41	42.3
4.	Shock	Present	54	43.9
		absent	69	56.1
5.	Cord blood pH	7-7.2	79	64.2
		<7	44	35.8
6.	HIE staging	HIE stage I	37	30.0
		HIE stage II	50	40.7
		HIE stage III	36	23.3
6.	Hospital stay	<7 days	36	23.3
		7 -14 days	63	51.2
		>14 days	24	19.5
7.	Outcome	Improved	105	85.3
		Expired	18	14.7

Table no 3: Cardiovascular parameter in study group

S.N.	Cardiovascular parameter	Number of newborn n= 123	Percentage %

1.	ECG grading	Normal	19	15.4
		Grade 1	17	13.8
		Grade 2	37	30.1
		Grade 3	40	32.5
		Grade 4	10	8.1
2.	CKMB level IU/L	<92.6	36	29.2
		92.6-150	05	4
		150-250	49	39.8
		>250	33	27.0
3.	Echocardiography	Normal	79	64.2
		Abnormal	44	35.8

Out of all neonates, 84.6% neonates showed abnormal ECG in the form of flat or inverted T waves on 1 or more limb leads or ST depression/elevation in chest leads or an abnormal Q-wave but none showed complete left bundle branch block. Most number of newborns (32.5%) had Grade 3 ECG changes. Echo was abnormal in 44 babies and all required ionotropic support for 1-5 days. Among the newborns, a significant proportion (70.7%) showed elevated CK-MB levels exceeding 92.6 IU/L. Notably, the majority of patients fell within the range of 150 to 250 IU/L.

Table no 4: Co-relation of cardiac parameter with HIE staging

s. no.	Cardiovascular parameter		HIE1 (n=37)	(%)	HIE2 (n=50)	(%)	HIE3 (n=36)	(%)	P value
1.	ECG grading	Normal	15	10.8	04	4	0	0	<0.01
		Grade 1	11	29.7	06	12	0	0	
		Grade 2	10	27	15	30	12	33.3	
		Grade 3	04	10.8	20	40	16	44.4	
		Grade 4	0	0	03	6	08	22.2	
2.	CKMB level IU/L	<92.6	23	62.2	08	16	5	13.9	<0.001
		92.6-150	03	8.1	02	4	0	0	
		150-250	09	24.3	27	54	13	36.1	
		>250	02	5.4	13	26	18	50	
3.	Echocardiography	Normal	35	95	31	62	13	36.1	<0.001
		Abnormal	02	5.4	19	38	23	63.9	

By applying Chi-square test we found that there was statistically significant difference in ECG findings, cardiac enzyme parameters and Echo findings amongst different grades of HIE. The difference in cardiac enzymes and Echo findings were more significant than the ECG findings in correlating with the severity of HIE.

Discussion

In the present study, cardiovascular involvement was there in 70.7% of neonates if we consider cardiac enzymes but only 63.9% babies were having abnormal echo findings. This was much higher as compared to the results obtained by Perlman et al.[9], Martín-Ancelet al.,[10] and Goodwin et al.[11] in their study. Other studies noted variable results.

In the present study, inotropes were required in 70 babies out of 123. All babies having abnormal Echo findings and most neonates having CK-MB levels exceeding 150 IU/L required inotropic support. 56.9% of the neonates in this study required inotropic support which is similar to the study conducted by Shah et al.,[13]in which 62% of the neonates required inotropes and Hankins et al.[14]who reported inotrope requirement in 61% neonates. Meanwhile, Martín-Ancel et al.[10] reported that 4% of their study neonates required inotropes.

In the present study, abnormal ECG was noted in84.6% of the neonates. Among these, 13.8% had grade I myocardial ischemic changes (as per Jedeikin criterion), 30.1%, 32.5% and 8.1% of neonates had grades II, III and IV myocardial ischemic changes respectively (as per Jedeikin criterion). In the study by Agrawal et al.[15] in 2012, ECG changes were observed in 76.7% neonates and the prevalence was similar to our study; 41.3% of whom had Grade I, 28.2% had Grades II and III each, and 2.1%had grade IV abnormalities.

Rajakumar et al. [16] reported ECG changes in almost similar percentage (73.3%) of cases. The most common finding in their study was “T” -wave inversion (36.7%) followed by “T” -wave flattening (33.3%), which is equivalent, to grade 1 ECG changes. We observed lower number of Grade I abnormalities and higher number of Grade II and III features. The presence of these ECG abnormalities suggests myocardial ischemia resulting from birth asphyxia in neonates.

In the present study, elevation of CK-MB was in70.7% of neonates. Our result differs vastly with the study by Hankins et al.[14] who noted elevated CK-MB values in only 17% neonates. Similar interpretation was also given by Primhak et al.[9] in their study who investigated serial electrocardiograms and CK-MB levels in term infants. They found an association between elevated CK-MB and myocardial injury in asphyxiated infants. Omokhodion et al. [17] in their research, explored the specificity of CK-MB as a marker for myocardial injury in asphyxiated newborns. However, they concluded that uncertainty remains regarding CK-MB’s precise role in this context.

Overall, 14.7% of study subjects died which is much lower than reported by Shah et al.,[13] who observed adverse outcomes in 64% of those with cardiovascular involvement. This may be due to the fact that 64.2% of our neonates have normal Echo, 29.2% have normal cardiac enzymes, 29.2% have normal ECG or Grade I abnormalities and only 56.9% babies required inotropes.

In our study, the overall mortality rate was 14.7%, which contrasts significantly with the findings reported by Shah et al.[13] They observed adverse outcomes in 64% of neonates with cardiovascular involvement. However, several factors may explain this difference like substantial proportion (64.2%) of our neonates had normal Echo results. Also, 29.2% of our neonates had normal cardiac

enzyme levels, 29.2% exhibited either normal ECG results or Grade I abnormalities and only 56.9% of the babies required inotropic support.

Conclusions

Myocardial ischemia in newborns is a well-recognized syndrome often associated with perinatal asphyxia. Despite the heart's 'preferential' perfusion, hypoxia leads to multiorgan damage, including myocardial injury. In our study, the combined insights from ECG, echocardiogram, and serum enzymes allowed reliable detection and grading of myocardial damage. Notably, cardiovascular dysfunction was prevalent among neonates following asphyxia, and those with compromised cardiac function had poorer outcomes. Early screening and robust cardiovascular support may enhance outcomes for neonates affected by asphyxia.

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Conflicts of interest

There are no conflicts of interest.

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