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Myocardial Dysfunction Caused by Perinatal Asphyxia in Full-term Infants

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Abstract

Background: Perinatal asphyxia may cause multiple organ dysfunctions, including myocardial dysfunction. This study aimed to evaluate the prevalence and features of myocardial dysfunction in perinatal asphyxia.

Methods: This study was carried out on 31 neonates (≥37 weeks) with perinatal asphyxia who were admitted to the Neonatal Intensive Care Unit (NICU). The neonates underwent Electrocardiography (ECG) and Echocardiography (ECHO) in the first 72 hours of birth. Moreover, in the first 24 hours of birth, 1 cc of blood was taken from the patients for cardiac troponin I (cTnI) and creatine kinase-myocardial band (CK-MB) testing. Following that, venous blood gas was recorded one hour later.

Results: The mean 1- and 5-min Apgar scores were 4±1.76 and 6.8±1.6, respectively. The mean value of serum cTnI was 4±1.76, and mean level of CK-MB was obtained at 136.51±258.51. ECGs were of grade 1. Mitral valve E-wave/Early diastolic (51%), followed by Tricuspid Regurgitation Vena Contracta (48.4%) was found to be the commonest ECHO abnormality, and Mitral annular plane systolic excursion (96.8%) was the most normal ECHO parameter. Infants with ECG grade 1 changes had a lower 5-min Apgar score (P=0.014), and higher serum cTnI level (P=0.002). ECG changes were not significantly correlated with the mean of Apgar at 1 min, umbilical vein PH, and CK-MB.

Conclusion: ECG and ECHO changes, serum troponin I level, and 5-min Apgar score were found to be the predictors for myocardial dysfunction caused by asphyxia in newborn infants.

Key Words: Birth asphyxia, Echocardiography, Electrocardiography, Myocardial changes, Neonate.

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1- INTRODUCTION

Perinatal asphyxia is a serious clinicopathological condition that occurs when the fetus or newborn is deprived of oxygen before or during birth due to hypoxic or ischemic insult (1, 2). Perinatal asphyxia is a leading cause of about a quarter of infant mortality and morbidity worldwide, especially in underdeveloped countries (3-5).

Perinatal asphyxia may result in the dysfunction of multiple organs, mostly the brain, kidneys, cardiovascular systems, and lungs (6). An asphyxiated neonate has umbilical vein blood pH <7.2, or the Apgar score of 5 for 10 minutes (7).

According to previous studies, the incidence of cardiac failure, as one of the most clinical presentations in asphyxiated neonates, is about 29%-78% (8). Some cardiovascular complications occurred during severe hypoxia among neonates with asphyxia include atrioventricular valve regurgitation, pulmonary hypertension, arrhythmia, hypotension, cardiogenic shock, and myocardial ischemia leading to cardiogenic shock (9-11).

Therefore, early identification of infants at risk of cardiac failure in perinatal asphyxia for the purpose of timely and appropriate management and essential interventions may improve the outcomes and prevents long-term consequences. Electrocardiography (ECG), echocardiography (ECHO), assay of biochemical markers, such as creatine kinase-myocardial band (CK-MB), and the cardiac troponin I (cTnI) were used for the diagnosis of cardiac dysfunction in perinatal asphyxia (12-14).

This study was designed and implemented to investigate the prevalence and features of myocardial dysfunction as one of the most common complications caused by perinatal asphyxia.

2- MATERIALS AND METHODS

2-1. Design and participants

This descriptive-analytical study was carried out on 31 neonates (≥37 weeks) with perinatal asphyxia who were admitted to the neonatal intensive care unit (NICU) of Qaem and Imam Reza hospitals, Mashhad, Iran, from 2020 to 2021.

2-2. Inclusion and exclusion criteria

Inclusion criteria were gestational age of ≥37 weeks, umbilical vein blood pH <7.2, and 1-min Apgar score < 7. On the other hand, infants with congenital anomalies, such as congenital heart diseases, and those who had syndromic appearance were excluded from the study.

2-3. Procedure

Neonates were examined in terms of clinical parameters upon admission at NICU and underwent electrocardiography and echocardiography in the first 72 hours. In addition, 1 ml of venous blood was taken from the patients in the first 24 hours for the estimation of the biochemical parameters of CK-MB and cardiac troponin I (cTnI). The serum cTnI levels were assessed quantitatively using ELISA (the exact name of the device). The normal range for cTnI in our lab is less than 0.01 µg/L. The serum level of CK-MB was estimated by enzymatic method with RA 1000 auto analyzer and normal values were considered less than 25 U/Lit.

12-lead serial ECG changes were used for the detection of any cardiac dysfunction. In the abnormal group, ECG is divided into the following grades based on the Jedeikin criteria (15).

Grade 1: Equivocal-Flat or inverted T wave in one lead only

Grade 2: Suggestive-Flat or inverted T in several leads with abnormal Q wave in any lead

Grade 3: Moderate-Flat or inverted T in several leads or Bundle branch blocks with abnormal Q plus abnormal ST segments

Grade 4: Severe-Classical segmental infarction pattern with abnormal Q waves and markedly elevated ST segments 2 D. Echocardiography with color Doppler was performed at the bedside in each neonate within 72 hours of life.

2-4. Data analysis

Data were analyzed using SPSS software (version 23.0). Mean±SD, frequency, and percentages were used for describing variables. Chi-square test, independent t-test, ANOVA, and Fisher's exact test were also used to compare the outcomes. A P-value of less than 0.05 was considered statistically significant.

3- RESULTS

3-1. General characteristics of asphyxiated neonates

Out of 31 neonates with asphyxia, 18 (58%) cases were male. The mean values of gestational age and birth weight were obtained at 38±6 weeks and 3278±512 (2070-4700) grams, respectively. Cesarean section was the most common (71%) mode of delivery. The mean hospital stay of newborns was 5.9±6.6 days, and most of them were hospitalized for less than a week. In total, 26 (83.9%) neonates required resuscitation and 10 (32.3%) infants needed ventilation.

Seizures observed in 6 (19.4%) patients, and 4 (12.9%) neonates required cardiovascular medication. Furthermore, 7 (22.6%) mothers used medication during pregnancy. Hypertension (5 mothers) and hypothyroidism (5 mothers) were the most common maternal diseases, followed by diabetes (4 mothers), addiction (3 mothers), and premature rupture of membranes (PROM) (2 mothers). More detailed information is given in **Table 1**.

3-2. The Apgar score

The mean Apgar scores at 1- and 5- min were 4±1.76 and 6.8±1.6, respectively (**Table 2**).

3-3. Venous blood gas

The mean level of umbilical vein pH was 7.12±0.17 at birth and 7.29±0.11 one hour after birth. The mean bicarbonate (HCO3) was 17.28±4.34 mmHg at birth and 18.34±3.88, one hour after birth (**Table 3**).

3-4. Biochemical parameters

The mean value of serum cTnI and mean level of CK-MB were determined at 4±1.76 and 136.51±258.51, respectively (**Table 5**).

3-5. ECG and ECHO analyses

Among 31 asphyxiated neonates, ECG was abnormal in 6 (19.4%) cases, all of these had grade 1; and abnormal ECHO was observed in 28 (90.3%) neonates.

As shown in **Table 7**, the mean RV TAPSE was estimated as 7.54±2.42, and the mean LV EF was obtained at 66.8±8.09 (%). AO VT1 in 8 (25.8%), TR PPG in 7 (22.6%), PI PPG in 7 (22.6%), TR VC in 15 (48.4%), PI VC in 7 (22.6%), MAPSE in 1 (3.2%), LV EPSS in 3 (9.7%), MV E/e in 16 (51.5%), MV E/A in 2 (6.5%), LV MPI in 2 (6.5%), RV MPI in 4 (14.3%), and RV ESD in 1 (3.2%) infants were abnormal. MV E/e` (51%), followed by TRVC (48.4%) was found to be the commonest ECHO abnormality, and MAPSE (96.8%) was the most normal ECHO parameter. Five asphyxiated neonates had patent arterial duct (PDA) and two had pulmonary hypertension.

Table-1: General characteristics of asphyxiated neonates and mothers

Variable	Category		Frequency (%)
Gender	Male		18 (58)
	Female		13 (42)
Delivery mode	Cesarean section		22 (71)
	Vaginal delivery		9 (29)
Causes of asphyxia	Infant distress		15 (48.4)
	difficult delivery		16 (51.6)
Resuscitation required	No		5 (16.1)
	Yes		26 (83.9)
Ventilation	No		21 (67.7)
	Yes		10 (32.3)
Seizure	No		25 (80.6)
	Yes		6 (19.4)
Need for cardiovascular medication	No		27 (87.1)
	Yes		4 (12.9)
Medication used during pregnancy	No		24 (77.4)
	Yes		7 (22.6)
Maternal disease history	No		17 (54.8)
	Yes		14 (45.2)
		Hypertension	5
		Diabetes	4
		Addiction	3
		Cardiovascular abnormality	1
		Multiple sclerosis	1
		Epilepsy	1
		Hypothyroid	5
		PROM	2
		Thrombocytopenia	1

Premature rupture of membranes (PROM)

Table-2: Apgar score of asphyxiated neonates

Variable	Mean±SD	Min-max
1-min Apgar score	4±1.76	1-8
5-min Apgar score	6.8±1.6	4-10

Table-3: Venous blood gas analyses

Variable	Umbilical vein	One hour after birth
PH	7.12±0.17	0.11±7.29
HCO3 (mmHg)	17.28±4.34	18.34±3.88
PCO2 (mmHg)	58.75±25.59	45.42±19.03

Table-4: Serum cTnI and CK-MB in asphyxiated neonates

Variable	Mean±SD	Min-max
cTnI	1.89±4.98	0.002-19
CK-MB	136.51±258.51	17-1121

Table-5: ECG and ECHO changes

Variable	Category	Frequency (%)
ECG changes	Normal Anormal	25 (80.6) 6 (19.4)
ECG grading	Grade 1 Grade 2 , 3 ,4	6 (19.4) 0
ECHO changes	Normal Anormal	3 (9.7) 28 (90.3)

Table-6: Echocardiographic findings in asphyxiated neonates

Variable	Mean±SD	Category	Frequency (%)
RV TAPSE (7)	7.54±2.42	Normal Abnormal	28 (98.3) 3 (9.7)
LV EF (%)	66.8±8.09	Normal Abnormal	29 (93.5) 2 (6.5)
AO VT1 (cm)	9.10±2.10	Normal Abnormal	23 (74.2) 8 (25.8)
TR PPG (mmHg)	21.19±15.33	Normal Abnormal	24 (77.4) 7 (22.6)
PI PPG (mmHg)	8.66±8.86	Normal Abnormal	24 (77.4) 7 (22.6)
TR VC (7)	5.03±6.08	Normal= mild (<3) Abnormal=moderate (3-7) and sever (>7)	16 (51.6) 15 (48.4)
PI VC (7)	1.8± 0.8	Normal Abnormal	24 (77.4) 7 (22.6)
MAPSE (7)	7.30± 1.26	Normal Abnormal	30 (96.8) 1 (3.2)
EPSS LV (7)	3.3± 0.8	Normal Abnormal	28 (90.3) 3 (9.7)
MV E/e	9.68± 8.6	Normal Abnormal	15 (48.4) 16 (51.6)
MV E/A	1.38± 1.1	Normal Abnormal	29 (93.5) 2 (6.5)
LV MPI	0.38± 0.05	Normal Abnormal	29 (93.5) 2 (6.5)
RV MPI	0.4± 0.05	Normal Abnormal	27 (87.1) 4 (12.9)
RV ESD (7)	15.9± 5.3	Normal Abnormal	1 (3.2) 30 (96.8)
PDA	-	-	26 (83.9) 5 (16.1)
Pulmonary hypertension	-	-	29 (93.5) 2 (6.5)

RV: Right Ventricular, TAPSE: Tricuspid annular plane systolic excursion, LV: Left ventricle ejection fraction, AO: Aortic valve, VTI: Velocity time integral, TR: Tricuspid Regurgitation, VC: Vena contracta, PPG: Peak-to-peak gradient, PI: Pulmonary insufficiency, MAPSE: Mitral annular plane systolic excursion, EPSS: E-Point to Septal Separation, MV: Mitral valve, E/e: E-wave/Early diastolic, E/A: E-wave/ Average e´, MPI: Myocardial Performance Index, EESD: End-systolic dimension, PDA: patent ductus arteriosus

Table-7: Association of echocardiographic findings with Apgar score, VBG PH, CK-MB, and cTnI

ECHO findings	1-min Apgar	5-min Apgar	VBG PH	CK-MB	cTnI
Normal	566±0.57	7.66±0.57	7.09±0.12	82.0±40.73	6.34±10.96
Abnormal	3.85±1.75	6.75±1.64	7.14±0.18	142.80±272.61	1.39±3.98
Total	4.03±1.76	6.83±1.59	7.14±0.17	136.51±258.51	1.89±4.93
P-value	0.062	0.259	0.547	0.351	0.522

Table-8: Association of ECG findings with Apgar score, VBG PH, CK-MB, and cTnI

ECG findings	1-min Apgar	5-min Apgar	VBG PH	CK-MB	cTnI
Normal	4.28±0.79	7.20±1.44	7.14±0.16	109.95±223.73	1.48±4.99
Abnormal	3.0±1.26	5.33±1.36	7.14±1.22	264.0±394.27	3.52±5.01
Total	4.03±1.76	6.83±7.14	7.14±0.17	136.51±258.51	1.89±4.93
P-value	0.099	0.014	0.707	0.132	0.002

3-6. Echocardiography findings, Apgar score, Venous Blood Gas PH, CK-MB, and cTnI

As shown in **Table 8**, no significant relationship of the Echo changes was observed with the mean Apgar at 1 min, Apgar at 5 min, venous blood gas (VBG) PH, CK-MB, and cTnI.

3-7. ECG findings, Apgar at 1 min, Apgar at 5 min, VBG PH, CK-MB, and cTnI

Table 9 shows the association of the mean serum cTnI level with 5-min Apgar score and ECG findings. Infants with grade 1 ECG changes had a lower 5-min Apgar score (P=0.014) and higher serum cTnI level (P=0.002), compared to infants with normal ECG. Additionally, babies with grade 1 ECG changes had higher values of CK-MB; however, the difference was not significant.

4- DISCUSSION

In this study, the prevalence and features of myocardial dysfunction were evaluated among infants with asphyxia admitted to the NICU of Qaem and Imam Reza hospitals, Mashhad, Iran.

Our results revealed that mean Apgar scores at 5 min were significantly lower in asphyxiated neonates who had abnormal ECG, compared to infants with normal ECG (P=0.014). This is in line with the findings of a study by Jain et al. (16). They found that mean Apgar scores at 1 and 5 min were significantly lower among the perinatal asphyxia group, compared to the control group (P<0.05 and P<0.001, respectively). Lakshmanan et al. (17) reported that the 5-min Apgar score was significantly low in non-survivors (P<0.001).

In our study, the mean level of CK-MB was 136.51±258.51 U/l, and its level was increased in 26 (83.3%) asphyxiated neonates. Some other studies demonstrated that the CK-MB was elevated in asphyxiated neonates (18-20). In the current study, although the mean level of CK-MB was higher in infants with abnormal ECG and ECHO results, no significant difference was observed between ECG and ECHO changes regarding CK-MB (P>0.05). In a study conducted by Kumar and Arasan (21), a statistically significant difference was reported between the normal and grade 4 ECG changes in terms of CK-MB level. Hence, CK-MB is not a reliable factor for the diagnosis of myocardial involvement in asphyxiated neonates. More studies are

needed regarding the importance of CK-MB in myocardial injury among neonates with asphyxia (18).

In the present study, the mean cTnI was 1.8±4.98 µg/L, and 6 (19.3%) asphyxiated neonates showed an elevated cTnI level. The results also indicated a significant relationship between ECG changes and cTnI (P=0.002). Infants with ECG changes had higher values of cTnI, compared to those with normal ECG. This finding is in line with the results of previously conducted studies (16, 22).

In this study, ECG was abnormal in 6 (19.4%) neonates, and all ECG changes were of grade 1. This is similar to the findings by Shakir et al. (18) who found abnormal ECG in 15.8% of asphyxiated neonates, of which 0.66% had grade 1. In a study conducted by Jain et al.(16), the ECG changes were seen in 67.75% of asphyxiated neonates, which is more than that in our results. They reported that grade 1 ECG changes were the most common abnormality which is comparable with those in our study. ECG changes showed no significant differences with the mean of umbilical vein blood pH, 1-min Apgar score, and CK-MB level.

After evaluating the ECHO findings, it was found that 28 (90.3%) and 3 asphyxiated neonates showed abnormal and normal ECHO results. The most abnormal parameters in echocardiography were Mitral valve E-wave/Early diastolic (51%) and Tricuspid Regurgitation Vena Contracta (49%); moreover, 93% of the normal infants (>60) had an ejection fraction. These results are comparable with the findings of a study by Jain et al. who reported tricuspid regurgitation as the most common (35.48%) valvular lesion, followed by mitral regurgitation (22.58%).

Yellanthoor and Dineshkumar reported echocardiographic changes in 45.6% of asphyxiated neonates, among them pulmonary artery hypertension with tricuspid regurgitation presented in 16 (28.1%) neonates was the main ECHO change. In another similar study, Herdy et al. (23) reported PDA in 20 (22%), tricuspid regurgitation in 6 (7%), pulmonary hypertension in 6 (7%), as well as dyskinesia and ventricular dilatation in 4 (5%) neonates. In a study by Afkhamzadeh et al. (24), 62% of the asphyxiated neonates had PDA. In the present study, pulmonary hypertension was observed only in 2 (6.5%) and PDA was found in 5 (16.1%) infants.

Moreover, differences of ECHO changes were not significantly correlated with the mean of umbilical vein blood pH, 1-min Apgar score, 5-min Apgar score, serum cTnI level, and CK-MB level.

4-1. Limitations of the study

This study didn’t focus on treatment in different stages of myocardial involvement. The lack of a control group for comparing the outcomes was another limitation of the study. More studies with comparative designs and larger sample sizes are, then, needed in this regard.

5- CONCLUSION

The results of this study indicated that most of the asphyxiated neonates had abnormal ECHO results. The most abnormal parameters in ECHO were Mitral valve E-wave/Early diastolic and Tricuspid Regurgitation Vena Contracta; moreover, ejection fraction was normal in most of the participants. The majority needed resuscitation. ECG changes were within grade 1. Furthermore, these changes were accompanied by higher values of cTnI and a lower 5-min Apgar score.

Hence, the ECG and ECHO changes, serum troponin I level, and 5-min Apgar score may be regarded as the predictors for myocardial dysfunction caused by asphyxia in newborn infants.

6- ETHICAL CONSIDERATIONS

The study was approved by the Ethics Committee of Mashhad University of Medical Sciences (IR.MUMS.MEDICAL.REC.1399.039), and written informed consent was obtained from the parents of the studied neonates.

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