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Original Article

Electrocardiographic and Echocardiographic Findings in Asphyxiated Neonates

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ABSTRACT

Background: The myocardium is vulnerable to ischemic injury in acute perinatal asphyxia. Asphyxial cardiomyopathy increases mortality. Clinical assessment alone is not sufficient to evaluate myocardial injury.

Methods: This study was conducted over 2 years on neonates at the gestational age of 34 weeks or more with perinatal asphyxia. Electrocardiographic (ECG) and echocardiographic changes were studied with clinical details.

Results: The study population comprised 57 neonates. Among them, 33 (57.9%) were male, 23 (40.4%) were born by cesarean section, and 3 (5.3%) were delivered via assisted vaginal delivery. Twenty-six neonates (45.6%) were intubated in the delivery room, and 15 (26.3%) required bag-and-mask ventilation at birth. The mean birth weight was 2679 g (461 g), and the mean gestation period was 38.4 weeks (1.6 wk).

Central nervous system, hepatic, and renal involvement was observed in 53 (93%), 35 (61.4%), and 26 (45.6%) cases, respectively. Cardiac dysfunction was observed in 30 neonates (52.6%). Twenty cases (35.1%) required mechanical ventilation.

ECG changes were observed in 44 neonates (77.1%). Grade I changes were observed in 10 cases (17.5%), Grade II in 14 (24.6%), and Grade III in 20 (35.1%). In 13 cases, ECG was normal. Twenty-six neonates (45.6%) had echocardiographic changes. Tricuspid regurgitation was observed in 8 cases (14%) and pulmonary artery hypertension with tricuspid regurgitation in 16 (28.1%). Mitral regurgitation with global hypokinesia was observed in 2 neonates, who eventually succumbed.

Conclusions: Our results demonstrated that ECG changes occurred in about three-fourths of asphyxiated neonates, and nearly half of the asphyxiated neonates had echocardiographic changes. Mitral regurgitation with global hypokinesia was associated with the worst outcome. ***(Iranian Heart Journal 2021; 22(2): 51-57)***

KEYWORDS: Perinatal asphyxia, Myocardial dysfunction, ECG, Echocardiography, Neonate

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Asphyxia is the leading cause of perinatal morbidity and mortality in developing countries. The incidence of perinatal asphyxia varies from 0.5% to 2% of live births. [1-5] In India, [1] 28.8% of all neonatal deaths were attributed to perinatal asphyxia as per the 2002-03 national neonatal-perinatal data. [1]

Most organs, including the myocardium, are vulnerable to ischemic injury in acute perinatal asphyxia. [5- 12] The incidence of cardiac dysfunction in perinatal asphyxia ranges from 24% to 78%. [1] Asphyxial cardiomyopathy results from ischemic myocardial damage and subendocardial infarction in some cases. [10-15] Ischemic cardiac damage decreases cardiovascular reserve and presents clinically with myocardial failure, bradycardia, hypotension, and elevated central venous pressure, which are associated with increased mortality and adverse neurological outcomes. [13-15]

Generally, the diagnosis of myocardial injury is based on clinical findings and creatine kinase (CK)-MB isoenzyme measurement. Clinical assessment alone, however, is inadequate to guide management or predict the outcome. The electrocardiographic (ECG) and echocardiographic patterns further help to study the extent of myocardial involvement. The increasing mortality rate has been correlated with asphyxia cardiomyopathy in asphyxiated neonates. [11, 12] In this context, we aimed to evaluate the ECG and echocardiographic findings in perinatally asphyxiated neonates as a marker of myocardial involvement. We also aimed to find out the association between these findings and immediate morbidity and mortality.

METHODS

This observational study was conducted over 2 years on newborns at the gestational age of 34 weeks or more with perinatal asphyxia admitted to the neonatal intensive care unit of Kasturba Hospital, Manipal. Demographic data, including age, sex, delivery mode, birth weight, and gestational age, were collected and recorded in a sheet designed for the study. The clinical examination findings, echocardiographic findings, ECG findings, inotrope use, evidence of the involvement of other systems in asphyxial insult, and outcomes until discharge were collected. Ethical approval was obtained from the institutional ethics committee, and informed consent was obtained from the neonates' parents. ECG was obtained using BPL Cardiart 6108 with a paper speed of 25 mm/s. Echocardiography was performed with the Philips CX-50 machine.

Neonates with perinatal asphyxia as per the criteria were enrolled in the study. Perinatal asphyxia was considered if the neonates satisfied any of the following criteria: not having cried or breathed at birth, requiring assistance for breathing at birth in the form of bag-and-mask or bag-and-tube ventilation with or without an Apgar score of 6 or less at 5 minutes, features suggestive of hypoxic encephalopathy (eg, seizure, hypotonia, coma, and irritability), cord blood pH of 7.0 or less, or neonatal arterial pH of 7.2 or less. Neonates with congenital heart defects, major congenital anomalies, and gestational age of less than 34 weeks were excluded. Neonates in whom ECG and echocardiography could not be obtained within 72 hours of life and those who died within 1 hour of life were also excluded.

Hypoxic-ischemic encephalopathy (HIE) was defined as a neonate with perinatal asphyxia having neurologic sequelae (ie, seizures, coma, and hypotonia) with or without profound metabolic or mixed acidemia (pH<7.00) in cord blood. HIE was further classified as Sarnat Stage I, Stage II, and Stage III based on clinical features. [2] Multiple-organ involvement was considered

when 2 or more organs; the kidney, central nervous system (HIE), lungs, liver, heart, or intestine; were involved. Bradycardia was defined as a heart rate of fewer than 100/min. Hypotension was defined as a systolic and/or diastolic blood pressure of equal to or lower than the fifth percentile for age and sex. A capillary filling time exceeding 3 seconds was considered an increased value.

ECG changes suggestive of myocardial injury were graded as per criteria defined by Jedeikin et al. [9] Grade I is defined as flat or inverted T- waves on 1 or 2 leads except for aVR. Grade II is defined as flat or inverted T-waves in 3 or more leads except for aVR. Grade III is defined as flat or inverted T-waves in 3 or more leads and either ST-depression or elevation exceeding 2 mm in at least 2 chest leads or exceeding 1 mm in at least 2 standard leads or a Q-wave abnormality of less than 0.02 seconds in duration or an amplitude of greater than 25% in the R-wave in 1 anterior or 3 related chest leads. Grade IV is defined as an abnormal Q-wave and a markedly elevated ST-segment or a complete left bundle branch block. Echocardiographic evidence of myocardial ischemia included any one of the following: tricuspid regurgitation, pulmonary artery hypertension with tricuspid regurgitation, mitral regurgitation, and right ventricular /left ventricular/global hypokinesia.

Renal dysfunction was defined as a creatinine level of more than the upper limit of the normal reference range for gestational age with or without a urine output of less than 1 mL/kg/h. [2] Hepatic dysfunction was defined as a transaminase level twice the normal level (normal aspartate transaminase up to 40 U/L and alanine transaminase up to 45 U/L).

The results were expressed as frequencies and percentages. The birth weight and gestation were expressed as the mean and the standard deviation (SD). The data analyses were performed using SPSS, version 16.0.

RESULTS

The study population comprised 64 neonates with perinatal asphyxia (Fig. 1). After the exclusion of 7 neonates, 57 neonates were further analyzed.

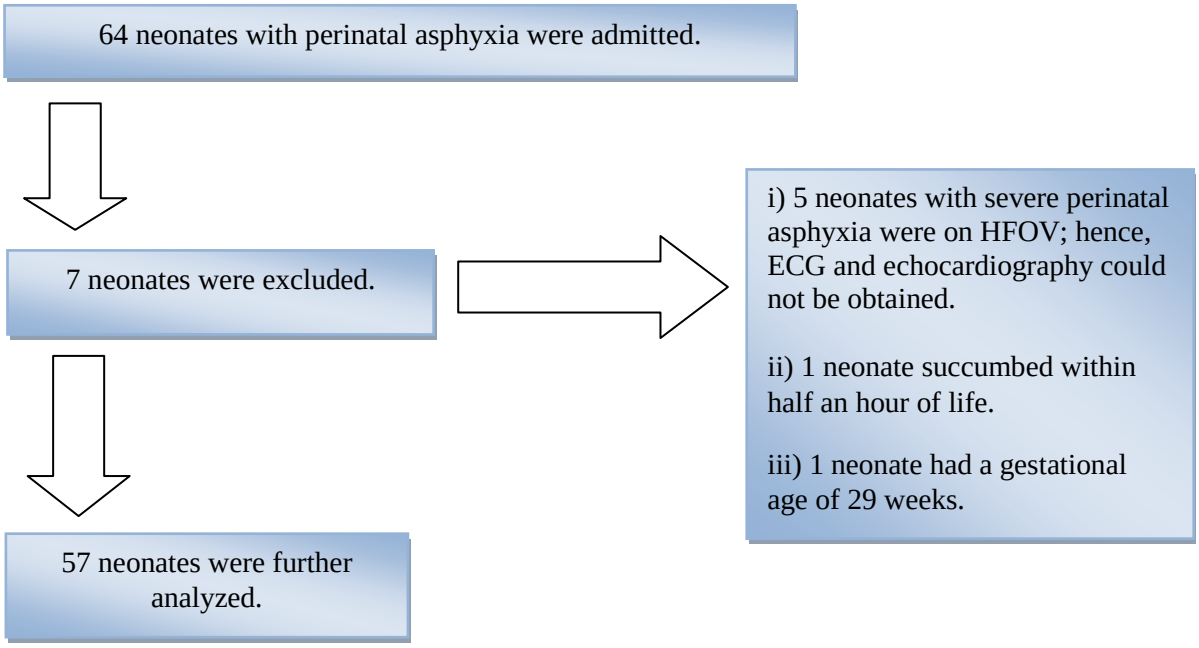

Figure 1: The flow diagram describes the study subjects.
ECG, Electrocardiography; HFOV, High-frequency oscillatory ventilation

Iranian Heart Journal; 2021; 22 (2)

Of the 57 neonates 33 (57.9%) were male, 23 (40.4%) were born by lower segment cesarean section (LSCS), and 3 (5.3%) were delivered using forceps or vacuum (Table 1). Among the 57 neonates, 26 (45.6%) were intubated in the delivery room and 15 (26.3%) required bag-and-mask ventilation at birth. The majority of the asphyxiated neonates (39 [68.4%]) had normal birth weight, and 12 (21.1%) neonates were late preterm. The mean birth weight was 2679 g (461 g), and the mean gestation age was 38.4 weeks (1.6 wk).

Table 1: Baseline characteristics of the neonates with perinatal asphyxia (N=57)

Characteristics	n(%)
Gender	
Male	33 (57.9)
Female	24 (42.1)
Mode of Delivery	
Vaginal	31 (54.4)
Assisted vaginal	3 (5.3)
LSCS	23 (40.4)
Mode of Resuscitation at Birth	
Free-flow oxygen	3 (5.3)
Bag-and-mask ventilation	15 (26.3)
Bag-and-tube ventilation	26 (45.6)
Not known	13 (22.8)
APGAR score at 5 min	
>6	3 (5.3)
≤6	18 (29.8)
Not known	37 (64.9)
Birth Weight	
2500-4000 g	39 (68.4)
1500-2499 g	18 (31.6)
Gestational Age	
34-36 wk	12 (21.1)
37-42 wk	45 (78.9)

LSCS, Lower segment cesarean section

Meconium-stained amniotic fluid was noted to be the most common antenatal risk factor associated with perinatal asphyxia (19.3%) (Table 2). Pregnancy-induced hypertension was found in 7 (12.3%) cases. In 25 cases (43.9%), there were no known antenatal complications. Fetal distress in the form of decreased fetal movements and fetal bradycardia was reported in 6 (10.5%) cases.

Table 2: Antenatal risk factors for perinatal asphyxia (N=57)

Risk factors	n	%
Meconium-stained amniotic fluid	11	19.3
Pregnancy-induced hypertension	7	12.3
Fetal distress	6	10.5
Antepartum hemorrhage	5	8.8
Cord around the neck	2	3.5
Breech delivery	1	1.8
No known antenatal complications	25	43.9

The most commonly involved organ in our neonates with perinatal asphyxia was the brain (53 [93%]). Cardiac dysfunction and hepatic involvement were observed in 30 (52.6%) and 35 (61.4%) cases, respectively. Renal dysfunction was found in 26 neonates (45.6%). About 20 cases (35.1%) required mechanical ventilation. Stage I, Stage II, and Stage III of HIE were observed in 7, 37, and 9 neonates, respectively. Six out of the 9 neonates with HIE Stage III died.

Table 3: Major organ involvement in the neonates with perinatal asphyxia (N=57)

Organ Involvement	n	%
Hypoxic-ischemic encephalopathy	53	93.0
Renal dysfunction	26	45.6
Cardiac dysfunction (Combination of ≥ 2 findings) Clinical Increased capillary filling time (27) Inotrope use (19) Fluid bolus need (27) Echocardiographic findings (26) Electrocardiographic findings (45)	30	52.6
Hepatic dysfunction	35	61.4
Lungs (requiring mechanical ventilation)	20	35.1

ECG changes were observed in 44 neonates (77.1%) with perinatal asphyxia (Table 4). Grade III and Grade II changes were more common. In 13 asphyxiated neonates, ECG was normal.

Table 4: ECG findings in the asphyxiated neonates (N=57)

ECG Findings	n	Percentage
Normal	13	22.8
Grade I	10	17.5
Grade II	14	24.6
Grade III	20	35.1
Grade IV	-	-

Of the 57 asphyxiated neonates, 26 (45.6%) had echocardiographic changes. Mitral regurgitation with global hypokinesia was observed in 2 neonates, who eventually succumbed. Inotropic support was required in 19 neonates. There were 9 neonates in whom both ECG and echocardiography were normal. Six neonates out of the 57 enrolled with perinatal asphyxia died.

Table 5: Echocardiographic findings in the asphyxiated neonates (N=57)

Findings	n	Percentage
Normal	31	54.4
Tricuspid regurgitation	8	14.0
Pulmonary artery hypertension with tricuspid regurgitation	16	28.1
Mitral regurgitation with global hypokinesia	2	0.04

DISCUSSION

Perinatal asphyxia in neonates leads to myocardial ischemia, which in turn contributes to morbidity and sometimes mortality. [15-20] The present study evaluated ECG and echocardiographic changes in perinatally asphyxiated neonates. ECG changes were observed in 44 cases (77.1%) with perinatal asphyxia, and 26 neonates (45.6%) had echocardiographic changes.

Of the 57 neonates evaluated, 33 (57.9%) were male, 23 (40.4%) were born by LSCS, and 3 (5.3%) were delivered using forceps or vacuum. A previous investigation on 60 neonates with asphyxia reported that among the neonates, 49 (81%) were male, 14 (23%) were delivered by LSCS, and 3 (5%) were born by vacuum or forceps. [15] Male preponderance (67%) among asphyxiated neonates was also reported in another study. [16] Meconium-stained amniotic fluid was noted as a common antenatal risk factor associated with perinatal asphyxia in the present study (19.3%). This risk factor has been reported by earlier researchers. [15-18]

Perinatal asphyxia involves multiple organs. [5-7, 18-24] In the present study, the central nervous system was involved in 93% of the neonates. Cardiac dysfunction and hepatic involvement were observed in 52.6% and 61.4% of the cases, respectively. Renal dysfunction was found in 45.6% of the neonates, and 35.1% required mechanical ventilation. Ana et al, [5] in their prospective study on 30 asphyxiated neonates, found the involvement of the central nervous system in 72%, renal involvement in 42%, cardiac involvement in 29%, and hepatic dysfunction in 26% of their study population. The involvement of the central nervous system reported in other studies ranges from 26% to 72% while renal system involvement ranges between 25% and 72%. [5-7, 15-18]

Cardiac involvement in perinatal asphyxia ranges from 29% to 78%. [2, 5-7, 15-18] Cardiac abnormalities in perinatal asphyxia include tricuspid regurgitation and mitral regurgitation associated with transient myocardial ischemia. Persistent hypoxia sometimes causes pulmonary arterial hypertension with consequent right-to-left shunts across the patent ductus arteriosus and the patent foramen ovale. Congestive cardiac failure, dyskinesia, and ventricular dilatation were also explained. Asphyxia leading to myocyte necrosis, congestion, vacuolization, and loss of striae was observed in necropsy. [22]

Various ECG changes due to myocardial involvement in perinatal asphyxia have been reported. [9, 11, 21] Severely asphyxiated newborns reflect relevant ischemic ECG changes and depressed left ventricular function. ECG changes were observed in 77.1% of the neonates with perinatal

asphyxia in the present study. Major changes in ECG were Grade II and Grade III. None of the study neonates had Grade IV changes. A previous study mentioned Grade I and Grade II changes in mild-to-moderate asphyxia and Grade III or Grade IV ECG changes only in severely asphyxiated neonates. [11] Herdy et al, [22] in their study on 90 asphyxiated neonates, reported that the main ECG findings were ST and T abnormalities. ECG abnormalities were reported in all 23 cases of severely asphyxiated neonates in another study. [25]

In the present study, 26 neonates (45.6%) had echocardiographic changes. The main change observed was pulmonary artery hypertension with mitral regurgitation. Mitral regurgitation with global hypokinesia was observed in 2 neonates, who were severely asphyxiated. Both of them had HIE Stage III and succumbed finally. Herdy et al [22] reported that echocardiography showed patent ductus arteriosus in 20 (22%), tricuspid regurgitation in 6 (7%), pulmonary hypertension in 6 (7%), and dyskinesia and ventricular dilatation in 4 (5%). Echocardiographic abnormalities in all severe cases of asphyxia and those with HIE Stage III were reported in another study. [25] Perinatal asphyxia not only affects cerebral blood flow but also alters cardiac function. A study evaluating the relationship between cardiac function and the cerebral blood flow velocity in term neonates with HIE using controls found that patients with left ventricular systolic dysfunction developed severe encephalopathy. [24] The severe grades of ECG and echocardiography changes are likely to be associated with the increasing severity of HIE and mortality. [25] Our findings suggest the utility of ECG and echocardiographic evaluation in asphyxiated neonates routinely, although the findings are limited by sample size.

CONCLUSIONS

Among 57 neonates with perinatal asphyxia, central nervous system, renal, cardiac, and hepatic involvement was observed in 53 (93%), 26 (45.6%), 30 (52.6%), and 35 (61.4%) cases, respectively. The fact that ECG changes occurred in about three-fourths of the asphyxiated neonates and that nearly half of the asphyxiated neonates showed echocardiographic changes indicates their role in understanding cardiac involvement in asphyxiated neonates better. Further, the association between mitral regurgitation with global hypokinesia and the worst outcome suggests the role of echocardiographic findings in prognostication as well as parental counseling.

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