Clinical and Laboratory Characteristics and Associated Factors to Mortality in Neonates with Birth Asphyxia: A Prospective Observational Study

Nguyen Thi Thanh Binh[1*], Vu Thi Dieu Huong[1,2], Tran Binh Thang[3]

(1) Department of Pediatrics, University of Medicine and Pharmacy, Hue University, Hue city, Vietnam
(2) Buon Ma Thuot University Hospital, Buon Ma Thuot Medical University, Ban Ma Thuot city, Vietnam
(3) Faculty of Public Health, University of Medicine and Pharmacy, Hue University, Hue city, Vietnam

Abstract

Aims: To describe the clinical and laboratory characteristics and to investigate associated factors with mortality of birth asphyxia. **Methods:** This was a prospective observational study conducted on a total of 120 asphyxiated neonates admitted to the Neonatal Intensive Care Unit (NICU). **Results:** Severe asphyxia was observed in 33.3%, and moderate asphyxia in 66.7% of the cases. The mortality rate was 19.2%. The common clinical features: apnea/gasping (45.8%), hypothermia (37.5%), lethargy (33.0%). The serious clinical signs: abnormal heart rate (15.8%), gastrointestinal bleeding (13.3%), oliguria and anuria (17.5%). The laboratory findings showed hypoglycemia (30.8%), elevated SGOT (45.0%), serum creatinine > 133 µmol/l (31.7%), hyponatremia (35.0%), hypocalcemia (65.8%), elevated lactate > 5mmol/l (53.6%). The factors that increased the risk of mortality in neonatal asphyxia were Apgar score at 5 min ≤ 5, seizure/coma, need for mechanical ventilation, serum creatinine > 133 µmol/l, liver injury, and lactate ≥ 5 mmol/l. **Conclusion:** The mortality rate is still high, and elevated serum creatinine, elevated liver enzymes, elevated lactate, and low 5-minute Apgar scores increase the risk of death in asphyxiated neonates.

Keywords: *birth asphyxia, mortality, risk factors, neonates.*

1. BACKGROUND

Neonatal asphyxia refers to the cessation of gas exchange between the mother and fetus through the placenta, either before, during, or immediately after birth, leading to the failure to initiate and sustain spontaneous breathing in neonates. Prolonged hypoxia can cause damage to multiple organ systems in neonates [1].

Despite advances in medical care, asphyxia remains a major cause of morbidity and mortality in the neonatal period. The incidence of perinatal asphyxia is approximately 2 per 1000 live births in developed countries, whereas it can be up to 10 times higher in developing countries, where access to maternal and neonatal health care is limited. Among neonates with asphyxia, 15-20% do not survive the neonatal period, and up to 25% of survivors may experience neurological impairment later in life [2].

Ischemic hypoxia in neonatal asphyxia can result in systemic effects, causing damage to multiple organs including the brain, heart, lungs, liver, kidneys, and gastrointestinal system. Brain injury is particularly severe and can result in irreversible neurological sequelae [1]. Therefore, prevention of asphyxia and prompt resuscitation within the first few minutes of life are the most effective measures to reduce the incidence and severity of asphyxia.

Additionally, in cases where asphyxia occurs, it is necessary to closely monitor the clinical features and perform laboratory tests to evaluate organ injury and disease progression. This allows for optimal management and improves the short-term and long-term prognosis of neonates. The objective of this study was to describe the clinical and laboratory characteristics of birth asphyxia and investigate factors related to mortality.

2. METHODS

Study design*:* this prospective descriptive study was conducted from May 2020 to July 2022 in the Neonatal Intensive Care Unit (NICU) of the Pediatric Center at the Hue Central Hospital, Hue City, Vietnam.

Study population: the study population consisted of a total of 120 asphyxiated neonates.

Birth asphyxia was defined as an Apgar score of less than 7 at 1 minute after birth, according to WHO criteria [3].

The Apgar score incorporates five components:

Corresponding author: Nguyen Thi Thanh Binh
Email: nttbinh.a@huemed-univ.edu.vn; nttbinh.med@hueuni.edu.vn
DOI: 10.34071/jmp.2023.6.8
Recieved: 24/7/2023; Accepted: 12/12/2023; Published: 31/12/2023

heart rate, respiration, muscle tone, reflexes, and skin color at 1 and 5 minutes after birth. The severity of asphyxia was classified as moderate (Apgar score between 4 and 6 at 1 minute after birth) or severe (Apgar score of 3 or less at 1 minute after birth).

The following exclusion criteria were applied: extremely preterm neonates (less than 28 weeks gestational age) or extramural newborns, and newborns with major congenital malformations, including severe congenital heart diseases or central nervous system anomalies.

Variables and Data collection:

The study collected demographic data, birth weight, gestational age, gender, Apgar score at 1 and 5 minutes, mode of delivery, and types of pregnancy. A complete clinical examination was performed on each neonate by neonatologists in the NICU at Hue Central Hospital. Biochemical parameters, including complete blood count, glucose level, serum electrolytes, serum creatinine, liver enzymes (SGOT, SGPT), serum lactate were collected at the time of admission after neonates had been stabilized respiratory and hemodynamic condition. Other imaging laboratory tests, including echocardiography and fontanel ultrasound, were also performed within the first 72 hours of life, and all results were recorded.

The survival status of asphyxiated neonates was determined at the time of discharge from the hospital.

Statistical analysis: Statistical analysis was performed using the Statistical Package for Social Sciences version 20.0. Qualitative variables were expressed as values (n) and percentages (%), while quantitative variables were analyzed by calculating the mean, median, and interquartile range. Univariate analysis of associated factors was conducted using chi-square. The odds ratio and 95% confidence interval for each possible risk factor were also calculated. A P-value of <0.05 was considered statistically significant.

Ethical Statements

The study was evaluated and approved by the Institution ethical committee for biomedical research of University of Medicine and Pharmacy, Hue University, Vietnam (No. H2020/129, dated: June 4th, 2020). Written informed consent was obtained from the parents of each neonate before enrollment.

3. RESULTS

Table 1. Basic characteristics of study population

Characteristics		(N = 120)	Percentage (%)
Gestational age (weeks)	< 34	16	13.4
	34 - < 37	43	35.8
	≥ 37	61	50.8
	Mean (X ± SD)	36.6 ± 2.5	
Gender	Male	71	59.2
	Female	49	40.8
Birth weight (grams)	< 2500	56	46.7
	2500 - < 4000	60	50.0
	≥ 4000	4	3.3
	X ± SD	2550 ± 792.1	
Types of delivery	Vaginal	28	23.3
	Caesarean section	92	82.7
Types of pregnancy	Twin or above	10	8.3
	Single	110	91.7
Severity of birth asphyxia	Severe	40	33.3
	Moderate	80	66.7
Outcome	Death	23	19.2
	Survival	97	81.8

A total of 120 asphyxiated neonates were included in the study, with a male/female ratio of 1.45/1. Among the neonates, 50.8% were term and 46.7% were low birth weight (< 2500 grams). The average neonatal weight was 2550 ± 792.1 grams. Severe asphyxia was observed in 33.3% and moderate asphyxia in 66.7% of the cases. The mortality rate was 19.2%. Table 1 summarizes the baseline characteristics of the study population.

Table 2. Clinical characteristics of asphyxiated neonates

Signs/symptoms		(N = 120)	Percentage (%)
Body temperature	Hypothermia	45	37.5
	Fever	0	0.0
Neurological system	Coma	4	3.3
	Seizure	15	12.5
	Lethargy	40	33.3
	Hypotonia	30	25.0
	Hypertonia	3	2.5
Skin	Cyanosis	25	20.8
	Pale/white	24	20.0
	Petechiae	22	18.3
Respiratory system	Need mechanical ventilation	55	45.8
	Breathing spontaneously	65	54.2
Cardiovascular	Heart rate < 100 bpm	9	7.5
	Heart rate > 160 bpm	10	8.3
	Refill ≥ 3s	14	11.6
Gastrointestinal system	Vomiting	11	9.2
	Abdominal distension	34	28.3
	Gastrointestional bleeding	16	13.3
	Enlarged liver	10	8.3
Kidney	Anuria	9	7.5
	Oliguria	12	10.0

The clinical and laboratory characteristics of the asphyxiated neonates are summarized in Tables 2 and 3. Among the asphyxiated neonates, clinical manifestations of neurological problems included coma (3.3%), seizures (12.5%), lethargy (33.3%), and decreased muscle tone (25.0%). Regarding the respiratory system, 45.8% of infants required mechanical ventilation (apnea/gasping), while 54.2% of neonates who breathed spontaneously showed respiratory distress, with 18.5% in severe respiratory distress, 63.0% in moderate respiratory distress, and 18.5% in mild condition. Various gastrointestinal symptoms were observed, including abdominal distention (28.3%), gastrointestinal bleeding (13.3%), vomiting (9.2%), and hepatomegaly (8.3%). Oliguria was present in 10.0% of neonates, while anuria occurred in 7.5% of cases. Our study also evaluated cardiac function, reporting that 5.9% of asphyxiated neonates had a reduced left ventricular ejection fraction (Table 2). Laboratory findings showed anemia (15.8%), hypoglycemia (30.8%), elevated SGOT > 100 U/l (45.0%), elevated SGPT > 100 U/l (3.3%), serum creatinine > 133 µmol/l (31.7%), hyponatremia (35.0%), hyperkalemia (10.8%), hypocalcemia (65.8%), and elevated lactate > 5 mmol/l (53.6%). Cerebral ultrasound performed through the anterior fontanelle revealed that 8.3% of asphyxiated neonates had intraventricular hemorrhage, while ventricular dilatation was observed in 1.7% of cases (Table 3).

Table 3. Laboratory characteristics of asphyxiated neonates.

Variables		N = 120	Percentage (%)
Hemoglobin (g/dL)	Hb < 13	19	15.8
	Hb > 13	101	84.2
	Trung vị (25^{th} - 75^{th})	16.2 (14.0 - 17.8)	
White blood cells (K/µL)	< 5	1	0.8
	5 - 25	86	71.7
	> 25	33	27.5
	Trung vị (25^{th} - 75^{th})	19.2 (13.7 - 26.9)	
Platelets (K/µL)	< 150	17	14.2
	≥ 150	103	85.8
	Trung vị (25^{th} - 75^{th})	244.0 (185.3 - 297.5)	
Glucose level	Hypoglycemia (< 2.6 mmol/l)	37	30.8
	Hyperglycemia (> 8.3 mmol/l)	9	7.5
SGOT (U/l)	Elevated (> 100 U/l)	54	45.0
	Normal (≤ 100 U/l)	66	55.0
	Median (25^{th} - 75^{th})	83.9 (49.4 - 145.0)	
SGPT (U/l))	Elevated (> 100 U/l)	4	3.3
	Normal (≤ 100 U/l)	116	96.7
	Median (25^{th} - 75^{th})	14.1 (9.2 - 28.3)	
Creatinin	Elevated > 133 µmol/l	37	30.8
	Normal ≤ 133 µmol/l	83	69.2
	Median (25^{th} - 75^{th})	87.4 (65.3 - 137.0)	
Sodium (mmol/l)	Hyponatremia (< 135)	42	35.0
	Normal (135 - 145)	76	63.3
	Hypernatremia (> 145)	2	1.7
	Median (25^{th} - 75^{th})	136.0 (133.0 - 139.0)	
Potassium (mmol/l)	Normal (< 6)	107	89.2
	hyperkalemia (> 6)	13	10.8
	Median (25^{th} - 75^{th})	4.3 (3.9 - 5.0)	
Calcium (mmol/l)	Hypocalcemia	79	65.8
	Normal	41	34.2
	Median (25^{th} - 75^{th})	1.1 (1.0 - 1.2)	
Lactate (mmol/l)	> 5	45	53.6
	≤ 5	39	46.4
	Median (25^{th} - 75^{th})	5.7 (3.0 - 10.5)	
Ejection Fraction (Echocardiography)	31 - 40%	2	1.7
	41 - 55%	5	4.2
	> 55%	113	94.1
Fontanel ultrasound	Intraventricular hemorhage	10	8.3
	Enlarged ventricles	2	1.7

We also investigated the factors associated with mortality in neonates with birth asphyxia, as summarized in Table 4. Our analysis revealed that several factors were significantly associated with an increased risk of mortality, including Apgar score at 5 minutes ≤ 5 (OR = 8.3 (3.0 - 22.7)), seizure/coma (OR = 3.1 (1.02 - 9.4)), need for mechanical ventilation (OR = 19.5 (4.3 - 87.9)), serum creatinine > 133 µmol/l (OR = 10.9 (3.8 - 31.2)), liver injury (OR = 8.4 (2.7 - 26.7)), and lactate ≥ 5 mmol/l (OR = 3.4 (1.1-10.5)). None of the variables such as gender, birth weight, gestational age, or Apgar score at 1 minute were found to be significantly associated with neonatal mortality (p > 0.05).

Table 4. Associated factors with mortality of birth asphyxia

Variables \ Outcome		Death (n = 23)		Survival (n = 97)		P- value	OR 95% CI
		N	%	N	%		
Gender	Male	14	60.87	54	55.67	0.651	0.8 (0.3 - 2.0)
	Female	9	39.13	43	44.33		
Gestational age (weeks)	≥ 37	18	78.3	86	88.7	0.195	2.0 (0.7 - 7.0)
	< 37	5	21.7	11	11.3		
Birth weight (grams)	< 2500	13	56.5	43	44.3	0.295	1.6 (0.7 - 4.1)
	≥ 2500	10	43.5	54	55.7		
Severity of asphyxia	Severe	11	47.8	29	29.9	0.105	2.1 (0.9 - 5.4)
	Moderate	12	52.2	68	70.1		
Apgar score at 5 minutes	≤ 5	16	69.6	21	21.7	< 0.001	8.3 (3.0 - 22.7)
	> 5	7	30.4	76	78.4		
Seizure/coma	Yes	6	26.1	10	10.3	0.045	3.1 (1.02 - 9.4)
	No	17	73.9	87	89.7		
Need mechanical ventilation	Yes	21	91.3	34	30.1	< 0.001	19.5 (4.3 - 87.9)
	No	2	8.7	63	64.9		
Creatinine (µmol/l)	> 133	17	73.9	20	20.6	< 0.001	10.9 (3.8 - 31.2)
	≤ 133	6	26.1	77	79.4		
SGOT and/or SGPT ≥ 100U/l	Yes	19	82.6	35	36.1	< 0.001	8.4 (2.7 - 26.7)
	No	4	17.4	62	63.9		
Lactate (mmol/l)	≥ 5	15	75.0	30	46.9	0.033	3.4 (1.1 - 10.5)
	< 5	5	25.0	34	53.1		

4. DISCUSSION

According to the WHO classification of birth asphyxia, the severity of asphyxia was defined based on the 1 minute-Apgar score. In our study, the incidence of moderate and severe asphyxia was 66.7% and 33.3%, respectively. The mortality rate among neonates with birth asphyxia was found to be high, with an overall rate of 19.2%. In severe cases, the mortality rate was 27.5% (11/40), while in moderate cases, it was 12% (12/80). Additionally, our findings indicated that the mortality rate observed in this study was similar to that reported by Thakkar et al. in India, which was 20% [4]. However, the mortality rate in the study by Yitayew et al in Ethiopia was higher, with 32% [5] .

Birth asphyxia can have systemic effects, and therefore, the clinical features of asphyxiated neonates can be diverse and involve almost all organ systems [6], [7]. In response to ischemic hypoxia in asphyxia, the circulation initiates important adaptive mechanisms by redistributing blood flow, reducing perfusion to organs such as the skin, kidneys, liver, and gastrointestinal tract to supply blood to vital organs such as the heart, brain, or

adrenal gland [1], [8]. However, if hypoxia is severe and prolonged, this compensatory mechanism fails, resulting in brain damage and the development of hypoxic-ischemic encephalopathy [1]. Previous studies have also reported these features in asphyxiated neonates, such as Ha Thi Kim Anh et al. who reported coma (7.3%), lethargy (51.2%), decreased muscle tone (34.1%), increased muscle tone (19.5%), and seizures (43.9%) [9] or Yitayew et al reported seizures (24.6%) [5]. In the study of Shen et al., 10% of cases presented lateral intraventricular hemorrhage at 72 hours postpartum, and 6.7% of cases showed both intraventricular hemorrhage and dilated ventricles [10]. Among the neurological signs of hypoxic-ischemic encephalopathy, seizures and coma are severe signs and are criteria in moderate or severe grades (grades II or III, respectively), according to the Sarnat and Sarnat scoring criteria of the disease [5]. Yitayew et al. also revealed that seizures are associated with an increased the risk of mortality in asphyxiated neonates about 1.52 times (with 95% CI: 1.02 - 2.27, $p < 0.05$), and the stage of asphyxia (moderate 3,5 times (with 95% CI: 1.55, 8.36) and severe, 11.55 time (with 95% CI: 4.73, 28.25) [5]. Thakkar et al. also found that seizures increase the risk of death in asphyxia ($p < 0.05$) and reported that neonates who had grade II or higher of HIE were associated with a poor prognosis in later life [4]. Thus, neurological examination is critical in asphyxiated neonates, which helps to evaluate neurological damage early as well as identify the stage of HIE, thereby performing intervention early to help reduce mortality and complications for neonates, especially in the first six hours after birth.

The hypoxia condition in asphyxia also causes pulmonary vasoconstriction, increased pulmonary vascular resistance, surfactant inactivation that leads to atelectasis, secondary respiratory distress syndrome, and persistent pulmonary hypertension [1]. In the study by Yellanthoor et al, 35.1% of cases required mechanical ventilation [11]. Since evaluation of respiratory function is necessary in birth asphyxia, optimal ventilation support and appropriate oxygen concentration are required to prevent prolonged hypoxia and minimize severe organ damage. Our study showed that asphyxiated neonates requiring mechanical ventilation had a 19.5 times higher risk of death than neonates with spontaneous breaths (OR: 19.5 (4.3 - 87.9), $p < 0.001$). Mohan et al also confirmed that timely mechanical ventilation reduces mortality in asphyxiated neonates [12].

Cardiovascular dysfunction in asphyxia is a consequence of ischemic myocardial injury and decreased blood volume. Clinical manifestations related to the cardiovascular system, such as heart failure, arrhythmia, hypotension, and shock, could increase mortality and neurological impairments in later life [8], [11]. Ischemia can cause damage to the lining of the digestive tract, leading to intestinal perforation and necrotizing enterocolitis. Furthermore, liver injury can occur due to low perfusion, and liver dysfunction is presented by increased expression of liver enzymes such as serum SGOT, SGPT, and coagulation disorders [1], [13]. In a study reported by Elsadek et al., the average value of SGOT and SGPT in asphyxiated neonates was higher than that in the control group (114.56 U/l and 90.44 U/l compared with 71.48 U/l and 28 U/l, respectively). This study also concluded that elevated liver enzymes were an indicator to determine the severity of asphyxia [13].

In the kidneys, prolonged hypoperfusion can result in acute tubular necrosis, acid-base and fluid-electrolyte disorders, and decreased glomerular filtration rate [1], [14]. In the kidneys, prolonged hypoperfusion can result in acute tubular necrosis, acid-base and fluid-electrolyte disorders, and decreased glomerular filtration rate [12]. Currently, acute kidney failure (AKF) is defined by urine volume and/or elevation of serum creatinine levels greater than 1.5 mg/dL (> 133 µmol/L) [14]. In the present study, 31.7% of neonates had creatinine levels greater than 133 µmol/L, while a lower incidence of 12.8% was reported in the study by Ashraf et al [7]. Compared to neonates without AKF, neonates with AKF had a 10.9 (95% CI 3.8 - 31.2, $p < 0.001$) times higher risk of mortality. Similar results were obtained in other studies. For example, Alaro et al demonstrated that AKF increases the risk of mortality in asphyxiated neonates, with an OR of 24 (95% CI 3.7 - 157, $p < 0.001$) [15]. In asphyxia, there may be inappropriate antidiuretic hormone secretion, delayed postpartum parathyroid hormone secretion, acidosis, and kidney failure that can affect the ingestion or elimination of electrolytes such as sodium, potassium, and calcium [16]. Therefore, electrolyte disorders including hyponatremia, hyperkalemia, and hypocalcemia are common in asphyxiated neonates [1]. These findings were in agreement with our study and other previous reports by Ashraf et al [7] and Shah et al [6].

Prolonged and severe hypoxia drives neonatal tissue towards anaerobic metabolism to produce energy, leading to an increase in serum lactate and metabolic acidosis[17]. Varkilova et al. reported

that the lactate level in the asphyxia group was significantly higher than that in the control group (5.3 +/- 3.4 mmol/L vs. 2.7 +/- 1.2 mmol/L, respectively) and that lactate level is a reliable tool to evaluate the severity of asphyxia. Additionally, elevated lactate levels after birth are a prognostic factor for severe hypoxic-ischemic encephalopathy [18]. In our study, elevated lactate was observed in 53.6% of neonates and those with lactate level ≥ 5 mmol/l had a 3.4 times higher risk of death than their counterparts (95% CI 1.1 - 10.5, $p < 0.05$).

Apart from the significant risk factors of mortality in asphyxiated neonates such as convulsions/ coma, requiring mechanical ventilation, elevated creatinine, elevated liver enzymes, and lactate≥ 5 mmol/l, we explored other potential factors and their association with neonatal mortality. Our study did not reveal any statistically significant association between gender, birth weight, gestational age, or Apgar at 1 minute with neonatal mortality. Thakkar et al similarly reported no significant association between gestational age, gender, birth weight, or need for mechanical ventilation with mortality [4]. However, our study demonstrated that a 5-minute Apgar score ≤ 5 was associated with an increased risk of death in asphyxiated neonates, with an odds ratio (OR) of 8.3 (95% CI 3.0 - 22.7, $p < 0.001$). Apgar score is a rapid and useful method of assessing the clinical status of newborns and the need for resuscitation at 1 minute of life, while the Apgar score at 5 minutes reflects the response to resuscitation. A lower 5-minute Apgar score suggests prolonged ischemia and hypoxia, which may lead to multiorgan dysfunction and increase the mortality risk in neonates with asphyxia. Therefore, prompt resuscitation immediately after birth is essential in cases of perinatal asphyxia to achieve effective and rapid recovery of newborns, minimize the risk of multiorgan damage, and improve short- and long-term outcomes for asphyxiated neonates. This finding is consistent with the results of a study by Yitayew et al, which also identified the severity of asphyxia as a significant predictor of mortality in neonates with asphyxia [5]. Hence, it is crucial to closely monitor and screen for severe asphyxia and multiorgan failure and manage them appropriately in the early period to minimize mortality in asphyxia, particularly in low- and middle-income countries where birth asphyxia is more prevalent.

5. CONCLUSION

A study involving 120 asphyxiated neonates revealed that asphyxia causes damage to multi-organs presenting in clinical and laboratory changes. Despite interventions, the mortality rate of asphyxiated neonates remained high at 19.2%. Factors such as seizures, coma, the need for mechanical ventilation, elevated levels of serum creatinine, SGOT/SGPT, and lactate, as well as low Apgar scores at 5 minutes, were significantly associated with an increased risk of mortality among neonates with asphyxia.

REFERENCES

1. Rainaldi MA and Perlman JM. Pathophysiology of birth asphyxia. Clinics in perinatology. 2016; 43(3): pp. 409-422.

2. Samad N, Farooq S, Hafeez K, Maryam M and Rafi MA. Analysis of consequences of birth asphyxia in infants: a regional study in Southern Punjab, Pakistan. Journal of the College of Physicians Surgeons Pakistan. 2016; 26(12): pp. 950-953.

3. World Health Organization. South East Asia Region, South East Asia Regional Neonatal-Perinatal Database. 2010; SEAR-NPD, 2007 - 2008

4. Thakkar PA, Valia P, Parmar N, Javadekar B, & Thakkar UP. Clinical profile, outcome and clinical indicators for poor prognosis in full term babies born with severe birth asphyxia: study from tertiary care hospital from western India. International Journal of Contemporary Pediatrics. 2017; 4(2), 470.

5. Yitayew YA and Yalew ZM. Survival status and predictors of mortality among asphyxiated neonates admitted to the NICU of Dessie comprehensive specialized hospital, Amhara region, Northeast Ethiopia. Plos one. 2022; 17(12): p. e0279451.

6. Shah GS, Agrawal J, Mishra OP, & Chalise S. Clinico-biochemical profile of neonates with birth asphyxia in eastern Nepal. Journal of Nepal Paediatric Society. 2012; 32(3): pp. 206-209.

7. Ashraf N. Clinico-biochemical profile in neonates with birth asphyxia. Journal of Islamabad Medical Dental College. 2017; 6(2): pp. 64-68.

8. Polglase GR, Ong T, and Hillman NH. Cardiovascular alterations and multiorgan dysfunction after birth asphyxia. Clinics in perinatology, 2016; 43(3): pp. 469-483.

9. Ton NVA, Ha TKA. Clinical characteristics at birth asphyxia infants. Y hoc Thanh pho Ho Chi Minh. 2015; Supplement of Vol. 19(3): pp. 202-206.

10. Shen W, Pan J-H, and Chen WD. Comparison of

transcranial ultrasound and cranial MRI in evaluations of brain injuries from neonatal asphyxia. International journal of clinical experimental medicine. 2015; 8(10): p. 18319.

11. Yellanthoor RB, Kumar DR. Electrocardiographic and Echocardiographic Findings in Asphyxiated Neonates. Iranian Heart Journal. 2021; 22(2): pp. 51-57.

12. Mohan K, Mishra P, and Singh D, Clinical profile of birth asphyxia in newborn. Int J Sci Tech. 2013; 3(1): pp. 10-9.

13. Elsadek AE, FathyBarseem N, Suliman HA, Elshorbagy HH, Kamal NM, Talaat IM, et al. Hepatic injury in neonates with perinatal asphyxia. J Global Pediatric Health. 2021; 8: p. 2333794X20987781.

14. Mok TYD, Tseng MH, Lee JC, Chou YC, Lien R, Lai MY, et al. A retrospective study on the incidence of acute kidney injury and its early prediction using troponin-I in cooled asphyxiated neonates. Scientific Reports. 2020; 10(1): p. 15682.

15. Alaro D, Bashir A, Musoke R, & Wanaiana L. Prevalence and outcomes of acute kidney injury in term neonates with perinatal asphyxia. J African health sciences. 2014; 14(3): pp. 682-688.

16. Thakur J, Bhatta NK, Singh RR, Poudel P, Lamsal M, & Shakya A. Prevalence of electrolyte disturbances in perinatal asphyxia: a prospective study. Italian journal of pediatrics. 2018; 44(1): pp. 1-6.

17. Mahmoud AT, Soliman MA, Saad AH and Abdelaziz AA. Study of blood levels of lactate, vitamin D, and nucleated red blood cells for hypoxic–ischemic encephalopathy prediction. Menoufia Medical Journal. 2021; 34(4): p. 1375.

18. Varkilova L, Slancheva B, Emilova Z, Nikolov A, Metodieva V, Hitrova S and Doicheva, E. Blood lactate measurments as a diagnostic and prognostic tool after birth asphyxia in newborn infants with gestational age> or= 34 gestational weeks. Akusherstvo i Ginekologiia. 2013; 52(3): pp. 36-43.