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Multiorgan dysfunction in birth asphyxia

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Abstract

Introduction: To obtain multi-organ dysfunction frequency, associated factors in neonates with birth asphyxia, and explore its relationship with short-term outcomes.

Methods: A prospective study included 120 asphyxiated neonates admitted to Hue Central Hospital, Vietnam. Central nervous system (CNS), renal, pulmonary, cardiovascular, liver, and gastrointestinal evaluations were conducted systematically.

Results: Of the asphyxiated neonates, 33.3% had severe asphyxia, while 66.7% had moderate asphyxia. Multiorgan dysfunction was observed in 55.8%, with involvement of two or more systems. CNS, pulmonary, liver, renal, cardiovascular, and gastrointestinal dysfunction occurred in 50.0%, 51.7%, 45.0%, 31.7%, 17.5%, and 13.3% of asphyxiated neonates, respectively. The overall mortality rate was 21.6%. Organ dysfunction was significantly associated with increased mortality, particularly respiratory, renal, and CNS dysfunction (odds ratios: 7.43, 6.56, and 5.92, respectively; p<0.001). Mortality risk increased with the number of affected organs/systems, with odds ratios of 41.33 and 5.52 for involvement of five and four organs, respectively (p<0.01). Severe asphyxia, Apgar score≤5 at 5 minutes, and elevated serum lactate levels (≥5 mmol/L) were significantly associated with multiorgan dysfunction (p<0.05).

Conclusions: Birth asphyxia in neonates often leads to multiorgan damage, increasing the risk of mortality. Preventive methods, prompt resuscitation, and systematic organ dysfunction screening are crucial to manage affected organs and improve outcomes.

Keywords: asphyxia; multiple organ failure; infant, newborn

1. INTRODUCTION

Birth asphyxia, a major cause of newborn mortality and morbidity, is caused by oxygen deprivation during labor and delivery [1]. It is defined as failure to establish spontaneous breathing at birth or an Apgar score of less than 7 at 1 minute of life [2]. Despite advances in screening and prenatal care, birth asphyxia remains a major problem worldwide, accounting for 4 to 9 million asphyxiated newborns per year [2]. It is ten times more common in developing countries than in developed countries, and it causes 1.2 million deaths and a significant number of survivors with serious medical conditions, such as cerebral palsy, epilepsy, and intellectual disabilities [3–6]. Therefore, it is important to reduce incidence and improve outcomes for asphyxiated neonates.

During birth asphyxia, the baby's blood flow and oxygen

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supply are reduced. To protect vital organs, including the brain, heart, and adrenal gland, blood perfusion to these organs is maximized. However, this reduced irrigation of other organs can lead to secondary injuries and multiple organ dysfunction (MOD). Birth asphyxia and subsequent MOD are associated with a higher risk of mortality, an increased burden of treatment, and severe long-term consequences [3],[4].

Most studies on neonates with severe birth asphyxia have evaluated its effects on the central nervous system (CNS) [7],[8]. Pattar et al. reported that all infants with hypoxic-ischemic encephalopathy secondary to severe asphyxia exhibited manifestations of dysfunction of at least one organ or system in addition to the CNS. Thus, perinatal asphyxia and subsequent MOD may be associated with a high risk of lifelong severe complications [8]. Fewer studies have investigated the involvement of organ systems other than the CNS, and most of these studies have focused on a single or two organs [9]. There was few available data in Vietnam on the effects of birth asphyxia on various organs of the body.

In Vietnam, asphyxia accounted for 2% of neonates admitted to a tertiary pediatric hospital (after sepsis, congenital diseases, jaundice, and prematurity). It also accounted for 40% of neonatal mortality in the first month of life [1]. The objective of this study was to describe the frequency of multiorgan dysfunction and identify the associated factors for multiorgan dysfunction following birth asphyxia; and to explore the association between multiorgan dysfunction and short-term outcomes in asphyxiated neonates.

2. METERIALS AND METHODS

2.1. Study settings

Study was conducted at the Pediatric Center of Hue Central Hospital, Vietnam. The Pediatric Center of Hue Central Hospital is a tertiary care hospital that provides comprehensive medical services for children from birth to 18 years old. The center offers a wide range of pediatric treatments.

2.2. Study design and participants

2.2.1. Study design

We conducted an observational prospective study of 120 neonates diagnosed with asphyxia in the Neonatal Intensive Care Unit (NICU) at the Pediatric Center of Hue Central Hospital, Vietnam between June 2020 and June 2022 (2 years).

2.2.2. Participants

The inclusion criteria were all infants born intramurally and admitted to the NICU. Asphyxiated neonates were identified using an Apgar score of less than 7 at 1 minute of age, according to the World Health Organization (WHO) criteria. The severity of asphyxia was defined as moderate if the Apgar score was between 4 to 6 at 1 minute of age and severe if the Apgar score was 3 or less at 1 minute of age [2].

The exclusion criteria included neonates with severe congenital malformations, inborn errors of metabolism, extremely preterm neonates (less than 28 weeks gestational age), and extramural neonates.

2.2.3. Variables and measurement

At the time of admission, we recorded the type of delivery, gestational age (<37 weeks, 37–42 weels, and >42 weeks), and nutritional status (small for gestational age [SGA], appropriate for gestational age [AGA], large for gestational age [LGA]).

In this study, we obtained asphyxiated neonates who were born in the obstetrics department and transferred to and admitted to the NICU after resuscitation in our hospital. At the time of admission, which typically occurs within the first hour of life, all babies underwent stabilization of their respiratory and hemodynamic conditions, and tests (glutamic-oxaloacetic transaminase [SGOT], serum glutamic pyruvic transaminase [SGPT], creatinine, lactate, glucose) were collected. Additionally, other bedside examinations, such as echocardiography, posterior fontanelle ultrasound, and abdominal X-rays, were performed within the first 24 hours.

We prospectively followed up the clinical course for the evaluation of multiorgan dysfunction in neonates with asphyxia.

The criteria for organ/system dysfunction were as follows [3],[4],[7],[8]:

CNS: Neonatal encephalopathy is indicated by decreased

consciousness, altered activities, reflexes, seizures, coma, abnormal tone, and sensorium. Hypoxic ischemia encephalopathy stage classification follows modified Sarnat and Sarnat criteria [3].

Pulmonary: Respiratory distress necessitating oxygen support ($FiO_2 \geq 40\%$) to maintain $SpO_2 > 92\%$ for the initial 24 hours or mechanical ventilation requirement.

Gastrointestinal: Signs include distention, tenderness, gastrointestinal bleeding, or necrotizing enterocolitis.

Renal: Criteria include anuria or oliguria (urine output<1 mL/kg/hr) lasting 24 hours or more, or serum creatinine>1.5 mg/dL (>133 µmol/L).

Liver: Elevated serum SGPT>100 U/L or serum SGOT>100 U/L within the first week after birth.

Cardiovascular: Poor perfusion signs encompass prolonged capillary refill time, weak pulses, tachycardia>160 bpm or bradycardia<120 bpm with or without hypotension, or hypotension requiring inotropes for over 24 hours to maintain normal blood pressure.

Multiorgan dysfunction was defined as those neonates had two or more organ dysfunction.

Short-term outcome was defined as either alive or dead during hospitalization until discharge.

2.3. Sample size and sampling

As multi-organ dysfunction outcome in asphyxiated neonates has not been reported in Vietnam, the sample size was derived based on the number of patients admitted to the hospital in the previous years. All patients admited to hospital within 2 years was included in our sample. We included all patients who met the inclusion criteria. As the results, 120 patients were included in our data analysis, which is a representative sample size for a tertiary care hospital in central Vietnam.

2.4. Statistical method

Statistical analysis was performed using SPSS version 20.0 (IBM, Chicago, IL, USA). Given the limited number of cases in our dataset, univariate binary logistic regression was utilized to determine possible associated factors of outcome and multiorgan dysfunction in asphyxiated neonates. Crude odds ratio and 95% Confident intervals 9CI) was presented. p-values <0.05 were considered statistically significant. We reported our paper following the STROBE guideline for prospective observational studies. Some missing information was not available in our study due to the cohort study design in a single group of patients [9] (Supplementary Table s1).

2.5. Ethical considerations

The study was assessed 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 from the parents of all neonates was obtained before selecting in the study.

3. RESULTS

A total of 120 asphyxiated neonates were included in the study. Out of these 120 neonates, 59.2% were males and 40.8% were females. The population study included 50.0% term neonates and 50.0% preterm neonates, with 92/120 (82.7%) babies delivered by Caesarean section. The mean gestational age was 36.6±2.5 weeks, and the mean birth weight was 2,550±7,92.1 grams. The general characteristics of the study population are shown in Table 1. In this study, the severity of asphyxia was evaluated by the Apgar score at 1 minute of life, and 40/120 (33.3%) neonates had severe asphyxia, while 66.7% had moderate asphyxia (Table 1).

In our study, CNS, pulmonary, liver, renal, cardiovascular, and gastrointestinal dysfunction was present in 50.0%, 51.7%, 45.0%, 31.7%, 17.5%, and 13.3% of neonates, respectively, as illustrated in Table 2. The results showed that 12.5% of neonates had no organ dysfunction, 31.7% had one organ/system injury, and 55.8% had multiorgan dysfunction with involvement of two or more organs or systems (Table 2).

Table 3 shows the association between organ dysfunction and the number of organ dysfunctions and outcome. The overall percentage of total mortality was 21.6% (26/120 neonates) for the study group. We found that neonates with one or more organ dysfunction were significantly associated with increased mortality. Respiratory, renal, and CNS dysfunction

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Table 1. General characteristics of study group

Variable	N=120	%
Gestational age (weeks)		
<34	16	13.4
34≤−37	44	36.6
≥37	60	50.0
Mean (X±SD)	36.6±2.5	
Gender		
Male	71	59.2
Female	49	40.8
Birth weight (grams)		
<2,500	56	46.7
2,500≤−4,000	60	50.0
≥4,000	4	3.3
X±SD	2,550±792.1	
Types of delivery		
Vaginal	28	23.3
Caesarean section	92	82.7
Nutritional status		
SGA	33	27.5
AGA	80	66.7
LGA	7	5.8
Severity of birth asphyxia		
Severe	40	33.3
Moderate	80	66.7

SGA, small for gestational age; AGA, appropriate for gestational age; LGA, large for gestational age.

Table 2. Incidence of organ dysfunction and multiorgan dysfunction in asphyxiated neonates (n=120)

Variable	N	Percentage (%)
Organ/system dysfunction (multiple-choice responses)		
Pulmonary	62	51.7
Central nervous system	60	50.0
Cardiovascular	21	17.5
Liver	54	45.0
Renal	38	31.7
Gastrointestinal	16	13.3
Number of organs/system dysfunction in asphyxiated neonates (per case)		
5	9	7.5
4	15	12.5
3	21	17.5
2	22	18.3
1	38	31.7
0	15	12.5

Table 3. Outcome of neonates with birth asphyxia

Organ/system dysfunction (ref=other)	Death N=26	Survival N=94	Crude OR 95% CI	p-value
Organ dysfunction in relation to outcome (multiple-choice responses)				
Pulmonary	22	40	7.43 (2.37–23.24)	<0.001
Central nervous system	21	39	5.92 (2.05–17.06)	0.001
Cardiovascular	9	12	3.62 (1.31–9.93)	0.0126
Liver	19	35	4.57 (1.74–11.97)	0.002
Renal	17	21	6.56 (2.55–16.85)	<0.001
Gastrointestinal	4	14	1.24 (0.36–4.23)	0.73
Number organ dysfunction in relation to outcome (per case)				
5	8	1	41.33 (4.86–351.05)	<0.001
4	8	7	5.52 (1.77–17.17)	0.0031
3	3	18	0.55 (0.14–2.04)	0.371
2	3	19	0.51 (0.14–1.89)	0.3185
1	4	34	0.32 (0.10–1.00)	0.051

OR, odds ratio; CI, confidence intervals; Ref, reference group; Other, defines as the other ogan/system or number of ogans of a group.

were associated with higher risks of death (odds ratio: 7.43; 6.56; and 5.92, respectively, with p<0.001). The results also show that the percentage of mortality of asphyxiated neonates could be different depending on which organ is injured. Indeed, the highest mortality was found in neonates with renal dysfunction (17/38 neonates or 44.7%), followed by cardiovascular dysfunction (9/21 neonates or 42.8%). Mortality increased as the number of organs/systems injuries increased from one to five. We observed 8/9 neonate deaths in the group with five (5) organs involvement and 8/17 neonate deaths in the group with four (4) organs involvement. Neonates who had five and four organs involved were associated with the risk of death (odds ratio 41.33 and 5.52, respectively, with p<0.01).

We also determined the association of multiorgan dysfunction with several clinical characteristics and laboratory of neonates with asphyxia (Table 4). We found that the Apgar score at 1 minute, Apgar score at five (5) minutes, and

Table 4. Univariable analysis of risk factor for multiorgan dysfunction in neonates with asphyxia

Variable	Multiorgan dysfunction				Crude OR (95% CI)	p-value
	Yes (n=67)		No (n=53)			
	N	%	N	%		
Gender						
Male	44	65.7	27	50.9	1.84 (0.88–3.85)	0.104
Female	23	34.3	26	49.1	Reference	
Gestational age (weeks)						
<37	32	47.8	28	52.8	0.81 (0.39–1.67)	0.581
≥37	35	52.2	25	47.2	Reference	
Birth weight (grams)						
<2,500	29	43.3	27	50.9	0.73 (0.35–1.51)	0.401
≥2,500	38	56.7	26	49.1	Reference	
Nutritional status						
SGA	19	28.4	14	26.4	1.11 (0.49–2.51)	0.801
AGA	44	65.7	36	67.9	Reference	
LGA	4	6.0	3	5.7	1.09 (0.23–5.20)	0.913
Apgar score at 1 minutes						
≤3	37	55.2	3	5.7	20.6 (5.8–72.5)	<0.001
>3	30	44.8	50	94.3	Reference	
Apgar score at 5 minutes						
≤5	36	53.7	1	1.9	60.4 (7.9–462.6)	0.0001
>5	31	46.3	52	98.1	Reference	
Glucose (mmol/L)						
<2.6	17	25.4	20	37.7	0.61 (0.27–1.35)	0.227
2.6–8.3	43	64.2	31	58.5	Reference	
>8.3	7	10.4	2	3.8	2.52(0.49–12.98)	0.268
Lactate (mmol/L)						
≥5	41	68.3	4	16.7	10.8 (3.2–35.9)	0.0001
<5	19	31.7	20	83.3	Reference	

OR, odds ratio; CI, confidence intervals; SGA, small for gestational age; AGA, appropriate for gestational age; LGA, large for gestational age.

lactate level were significantly associated with multiorgan dysfunction ($p<0.05$). Based on this study, severe asphyxia was linked to an increased risk of multiorgan dysfunction compared to moderate asphyxia (odds ratio: 20.66, 95%CI 5.8–72.5; $p<0.001$). Asphyxiated neonates with an Apgar score of five (5) or less at five (5) minutes had a 60.4 times increased risk for multiorgan dysfunction. Lactate levels equal to or more than five (5) mmol/L were associated with a greater incidence of multiorgan dysfunction (odds ratio: 10.8; 95%CI (3.2–35.9); $p<0.001$). However, other variables, including gender, gestational age, birth weight, nutritional status, and glucose level, were not associated with the multiorgan dysfunction condition in asphyxiated newborns ($p>0.05$).

4. DISCUSSION

This study explores the association between birth asphyxia and multi-organ dysfunction. Prolonged hypoxia resulting from reduced blood flow can lead to damage in various organs, including the CNS, respiratory, cardiovascular, gastrointestinal, liver, and renal systems… [1]. Previous studies have also documented similar findings in asphyxiated neonates. For instance, Martín-Ancel et al. conducted research

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in Spain and reported that the CNS was the most affected organ (72%), followed by renal (42%), cardiovascular (29%), and respiratory systems (26%) [10]. Likewise, Ashraf et al. in Pakistan observed involvement of the respiratory (71.8%), cardiovascular (25.6%), renal (12.8%), and gastrointestinal (5.1%) systems [8]. Similarly, Singh et al. in Sri Lanka reported renal injury as the most common (64%), followed by respiratory (45%) and cardiovascular (32%) damage [11].

In our current investigation, evidence of organ or system dysfunction was observed in 87.5% of asphyxiated neonates. Among them, 55.8% exhibited involvement of two or more organ systems, and 7.5% experienced damage to five organs. These rates align with previous research conducted by Martín-Ancel et al. [10], Ashraf [8], and Pattar et al. [12], which also reported similar rates of organ dysfunction in cases of neonatal asphyxia. Importantly, our study revealed that neonates with injury to any organ, except the gastrointestinal system, faced an increased risk of death ($p<0.05$). Moreover, mortality rates escalated as the number of involved organs increased from one to five. Most other studies have also established an association between individual organ/system dysfunction and mortality rate [4],[12]. Our findings specifically indicated that neonates with asphyxia and four or more organ dysfunctions had a statistically significant increased risk of death ($p<0.01$). These results are consistent with the findings by Pattar et al., who reported high mortality rates in asphyxiated neonates with neurological, respiratory, liver, and renal dysfunction (14%, 14.1%, 13.9%, and 7.5%, respectively) [12].

Our study specifically revealed that neonates with severe asphyxia, indicated by Apgar scores of five (5) or less at five (5) minutes, or elevated serum lactate levels of five (5) mmol/L or more, faced a significantly higher risk of developing multi-organ dysfunction. However, we found no significant correlation between multi-organ dysfunction and factors such as gender, gestational age, birth weight, nutritional status, or blood glucose levels in asphyxiated neonates. Interestingly, Martín-Ancel et al. reported that Apgar scores at one (1) and five (5) minutes were the only factors associated with multi-organ dysfunction in neonates with asphyxia, with an Apgar score of less than five (5) at five (5) minutes being closely linked to the number of organs injured (OR=17.5, 95% CI 4.58–66.9) [10]. Similarly, Shah et al. noted that multi-organ dysfunction was more prevalent in neonates with severe asphyxia, increasing the risk of death and long-term complications in surviving infants [4]. On the other hand, Ashraf N et al. found that although the incidence of multi-organ dysfunction was higher in the severe asphyxia group compared to the mild and moderate asphyxia group, the difference was not statistically significant ($p=0.064$) [8].

The Apgar score at five (5) minutes, particularly the change in score between one (1) minute and five (5) minutes, serves as a valuable indicator for evaluating the effectiveness of resuscitation efforts and predicting the risk of organ dysfunction, prognosis for survival, and sequelae in neonates [13]. A lower Apgar score at five (5) minutes indicates a higher likelihood of long-term hypoxia and subsequent organ damage. Prolonged tissue hypoxia leads to anaerobic metabolism, resulting in increased acidosis and lactate levels [14]. Elevated lactate levels are a risk factor for severe asphyxia and significantly higher mortality in neonates born with asphyxia. Therefore, the timing, quality, and effectiveness of resuscitation of newborns with asphyxia right after birth improves Apgar scores at five (5) minutes, consequently reducing the risk of multi-organ damage and mortality rates.

The incidence of multi-organ failure is directly correlated with the severity of asphyxia. Recognizing the high incidence of organ involvement emphasizes the need for screening organ function in cases of asphyxia as early as possible. The association between multi-organ failure and the Apgar score at five (5) minutes reinforces the importance of early intervention, such as neonatal resuscitation in the delivery room, in improving short-term and long-term outcomes for neonates with asphyxia. Early identification of organ dysfunction following perinatal asphyxia insults enables the establishment of optimal management strategies for these neonates.

While this is the first study of its kind in the region, it is important to acknowledge the limitations of the research. The study recorded the number of newborns over a two-year follow-up period. However, the new patient data only reflects a representative sample of the surrounding provinces

of the research hospital. Therefore, the results cannot be generalized to other provinces and cities and to the whole country. Additionally, the crude odds ratio estimates from the univariate analysis should only be interpreted as reflecting the association for each risk group with the outcome (death/survival) without adjusting for the interaction and confounding effects of other factors. Nevertheless, the findings of this study provide a foundation for future multicenter research with larger sample sizes in Vietnam and more in-depth statistical analyses of these causal relationships between multiple organ dysfunction and neonatal asphyxia outcomes. This could lead to valuable clinical recommendations.

5. CONCLUSION

In neonates experiencing asphyxia, the occurrence of multi-organ damage is prevalent, thereby heightening the risk of infant mortality. Asphyxiated neonates with prolonged hypoxia (indicated by Apgar scores less than five (5) at five (5) minutes) and elevated lactate levels are at high risk for multiple organ damage. Preventive measures, prompt resuscitation, and systematic organ dysfunction screening are crucial manage affected organs and improving outcomes.

SUPPLEMENTARY MATERIALS

Supplementary materials are only available online from: https://doi.org/10.32895/UMP.MPR.8.2.12

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Conflict of interest

No potential conflict of interest relevant to this article was reported.

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Availability of data and material

Upon reasonable request, the datasets of this study can be available from the corresponding author.

Ethics Approval

The study was assessed 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 from the parents of all neonates was obtained before selecting in the study.

REFERENCES

1. Kruse AY, Ho BTT, Phuong CN, Stensballe LG, Greisen G, Pedersen FK. Prematurity, asphyxia and congenital malformations underrepresented among neonates in a tertiary pediatric hospital in Vietnam. BMC Pediatr. 2012;12:199.
2. World Health Organization. South East Asia region, South East Asia regional neonatal-perinatal database. 2010: SEAR-NPD, 2007–2008. Geneva: World Health Organization; 2016.
3. Sarnat HB, Flores-Sarnat L, Fajardo C, Leijser LM, Wusthoff C, Mohammad K. Sarnat grading scale for neonatal

encephalopathy after 45 years: an update proposal. Pediatr Neurol. 2020;113:75-9.
4. Shah P, Riphagen S, Beyene J, Perlman M. Multiorgan dysfunction in infants with post-asphyxial hypoxic-ischaemic encephalopathy. Arch Dis Child Fetal Neonatal Ed. 2004;89(2):F152-5.
5. Tuan VM, Nhu BTH, Nhi NBM, Tuan TD. Post-delivery brachial plexus injury in neonates: a case series. MedPharmRes. 2019;3(1):8-11.
6. Tri DH, Tuan TD, Han NBH. The Vietnamese version of the health-related quality of life measure for children with epilepsy (CHEQOL-25): reliability. MedPharmRes. 2017;1(1):9-14.
7. Alaro D, Bashir A, Musoke R, Wanaiana L. Prevalence and outcomes of acute kidney injury in term neonates with perinatal asphyxia. Afr Health Sci. 2014;14(3):682-8.
8. Ashraf N, Butt N, Munir S, Zahid M, Fatima K, Minhas A. Clinico-biochemical profile in neonates with birth asphyxia. J Islamabad Med Dent Coll. 2017;6(2):64-8.
9. von Elm E, Altman DG, Egger M, Pocock SJ, Gøtzsche PC, Vandenbroucke JP. The strengthening the reporting of observational studies in epidemiology (STROBE) statement: guidelines for reporting observational studies. Lancet. 2007;370(9596):1453-7.
10. Martín-Ancel A, García-Alix A, Gayá F, Cabañas F, Burgueros M, Quero J. Multiple organ involvement in perinatal asphyxia. J Pediatr. 1995;127(5):786-93.
11. Singh V, Shrikhande CDY, Vohra R, Garg A. Organ dysfunction other than central nervous system in perinatal asphyxia. Sri Lanka J Child Health. 2018;47(2):141-5.
12. Pattar RS, Raj A, Yelamali BC. Incidence of multiorgan dysfunction in perinatal asphyxia. Int J Contemp Pediatr. 2015;2(4):428-32.
13. Yitayew YA, 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):e0279451.
14. Rainaldi MA, Perlman JM. Pathophysiology of birth asphyxia. Clin Perinatol. 2016;43(3):409-22.