

Characteristics of Neonatal Asphyxia in Perinatology Ward Sanglah General Hospital Denpasar

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Abstract: Background: Neonatal asphyxia is the failure of spontaneously and regularly breathe soon after birth. Birth asphyxia remains one of the top ten conditions responsible for neonatal death in Indonesia. Objective: To determine the characteristics and comorbid factor Neonatal Asphyxia in Perinatology Ward Sanglah General Hospital, Denpasar, Bali. Methods: This is a retrospective cross-sectional study with descriptive design. Data were collected from medical records of neonatal asphyxia patient during 2019. Results: Fifty neonates with neonatal asphyxia were included in this study. Subject were dominated by male (58%) with gestational age < 37 week or premature (72%), small gestational age (78%), birth weight <2500 gram (44%), lower ANC (82%), moderate asphyxia (64%), mother age >35 years old (68%), sectio caesaria delivery (64%), referral (74%) and higher mother education (82%). The characteristic comorbid factor of asphyxia were respiratory distress syndrome (78%), and hypoglycemia (86%). Conclusion: The characteristic of neonatal asphyxia in our center are dominated by male, low birth weight, gestation age < 37 weeks, with caesaria delivery, small gestational age, mother with age >35 years old and low quality of ANC. Our subjects also tend to characteristic comorbid factor of asphyxia which consist of a respiratory distress syndrome and hypoglycemia

Keywords: Characteristic, Asphyxia, Ante Natal Care

1. Introduction

Neonatal asphyxia is the failure of spontaneously and regularly breathe soon after birth. Identification can be done through observation of health condition of newborn immediately after birth, using the APGAR method. Assessment of APGAR scores include: skin color (Appearance), pulse (Pulse Rate), reaction to stimulant (Grimace), muscle tone (Activity), and breathing effort (Respiration).¹ This assessment is necessary to determine whether the infant is suffering asphyxia or not. Scores 0 - 3 at minute 5 shows the condition of severe asphyxia in infants and in more severe conditions can lead to death and other complication.²

According to World Health Organization (WHO), 4 millions deaths yearly occurred due to birth asphyxia, representing 38% of all deaths of children under 5 years of age. In low-income countries 23% of all neonatal deaths occurred due to birth asphyxia.³ According to a survey conducted by WHO in 2005, it is also one of the leading causes of neonatal deaths within first week of life.³ It is strongly associated with 1.1 million intrapartum still births and is responsible for long-term neurological disability and impairment.³

Causes of perinatal birth asphyxia may be prenatal, intranatal and postnatal. Those who survive may have chance to develop neurological complications including epilepsy, cerebral palsy and developmental delay.⁶ Risk factors from prenatal include maternal age, non attendance for antenatal care, and preeclampsia. Risk factors from intranatal include prolonged rupture of membranes, antepartum bleeding, placenta previa, solution placenta, delivery with caesarian section, vacuum extraction. Risk factor from postnatal include low birth weight infants, prematurity, and Intra Uterine Growth Retardation (IUGR).⁷

^{8, 9} Poor prognostic factors are repeated seizures, APGAR score of ≤ 4 at 10 minutes or later, hypoglycemia and hypothermia.⁸

Almost a half of birth number experienced asphyxia in Indonesia.⁷ Low birth weight case in Sanglah General Hospital Denpasar in 2018 was about 41%. It was in line with the increase of asphyxia case and sepsis neonatorum.⁴ Neonatal mortality is still a problem in Indonesia, especially in Sanglah General Hospital, Denpasar, Bali. The neonatal mortality rate in Sanglah Hospital in 2019 is 28.2%. neonates died with sepsis (67.57%), prematurity (9, 9%) severe asphyxia (5, 41%).^{4,7} It is necessary to know what factors can cause asphyxia.

2. Material and Methods

This study was a retrospective descriptive study with a cross-sectional approach to know the characteristics of neonatal asphyxia in the neonatal ward (level II - III) of the Sanglah General Hospital, Denpasar. Data was collected between January to December 2019. The inclusion criteria in the case group were neonate who diagnosed clinically neonatal asphyxia. Exclusion criteria in the case group if incomplete medical record data. Calculation of sample size using the single sample proportion formula in one measurement, with a significance level of 0.05 and a power of 80%. After being included in the formula, the total number of samples was 50 samples.

This research has received permission from the ethics committee of the Faculty of Medicine, Udayana University with the ethical clearance number 993/UN14.2.2.VII.14/LT/2021. The data of this study include data on the characteristics neonatal asphyxia and the comorbid factors for neonatal asphyxia.

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Neonatal asphyxia is the failure of spontaneously and regularly breathe soon after birth. Identification can be done through observation health condition of newborn immediately after birth, using the APGAR method. Assessment APGAR scores include: skin color (Appearance), pulse (Pulse Rate), reaction to stimulant (Grimace), muscle tone (Activity), and breathing effort (Respiration). Scores 0 - 3 at minute 5 shows the condition of severe asphyxia in infants, scores 4 - 6 at minute 5 shows the condition of moderate asphyxia in infants. Gender is the sex of the neonate based on phenotype, divided into male and female. Birth weight is weight of the baby weighed immediately after birth in gram, divided into normal birth weight >2500 gram, low birth weight <2500 grams.¹¹ Premature birth was determined based on gestational age < 37 weeks and not premature if gestational age 37 weeks. Weight for Gestational age defined as a birth weight based on Lubchenco kurve. This can divide that Small Gestational Age (SGA) defined as birth weight 2 standard deviations below the mean weight for gestational age or below the 10th percentile for gestational age, Appropriate for gestational age (AGA). Defined as a birth weight between the 10th and 90th percentiles for the infant's gestational age and Large for gestational age (LGA) defined as birth weight 2 standard deviations above the mean weight for gestational age or above the 90th percentile for gestational age. Ante Natal Care (ANC) is comprehensive health supervision of a pregnant women. Quality of ANC assessed on the frequency and standard of ANC. There are classified to adequate (at least 4 visits and get at least seven standard ANC) and lower ANC (less than 3 visit or never).^{3,7} Maternal age is the age of the mother at the time of delivery¹¹, divided that >35 years old and < 35 years old. Hypothermia is an abnormal thermal stage in which the newborn body temperature drops below 36, 5 C.¹⁰ Temperature recorded within 15 min of delivery or after resuscitation of neonate and recorded using a digital axillary thermometer. The infant with respiratory distress exhibits tachypnea, grunting, nasal flaring, and retractions of the chest wall, and may have cyanosis in room air.¹¹ This include hialin membrane disease, pneumonia neonatorum, meconium aspiration syndrome. The determination of respiratory distress based on clinically adjustment. The data presented in the form of nominal scale that are yes or no.

The data will be analyzed with SPSS program, variable categorical are described in the number and percentages presented in the form of the table and narrative.

3. Result

There were a hundred data neonatal asphyxia. Fifty neonates with neonatal asphyxia were included in this study and fifty data were excluded because of incomplete data. Data collected consists of demography, laboratory results. The characteristics of the study can be seen at the table 1.

Table 1 showed the subjects dominated by male (58%) with gestational age < 37 week or premature (72%), weight for gestational age is small gestational age (78%), birth weight <2500 gram (44%), lower ANC (82%), and 32 subject (64%) with moderate asphyxia. There was 34 (68%) mother age, >35 years old and higher mother education (82%). In

this study found that mostly the mother was sectio caesaria delivery (64%), there is no preeclampsia (70%), there is no premature rupture of membrane (82%), there is no antepartum bleeding (90%) and referral (74%).

Table 2 showed characteristic comorbid factor of asphyxia which consist of a hypothermia, respiratory distress syndrome and hypoglycemia. There was respiratory distress syndrome (78%), and hypoglycemia (86%).

Table 1: The Characteristics socio-demographic of the study

Variables	N = 50
Prenatal factor	
Mother age	
<35 years old	16 (32)
> 35 years old	34 (68)
Quality of ANC	
Low	41 (82)
Adequate	9 (18)
Preeclampsia	
Yes	15 (30)
No	35 (70)
Intranatal factor	
Premature rupture of membrane	
Yes	9 (18)
No	41 (82)
Antepartum Bleeding	
Yes	5 (10)
No	45 (90)
Delivery mode	
Spontaneous	18 (36)
SectioCaesaria	32 (64)
Postnatal factor	
Gender	
Male	29 (58)
Female	21 (42)
Birth weight	
<2500 gram	37 (68)
>2500 gram	13 (26)
Gestation age	
< 37 weeks	36 (72)
>37 weeks	14 (28)
Weight for Gestational age	
Small gestational age	39 (78)
Appropriate gestational age	8 (16)
Large gestational age	3 (6)
Outcome	
Life	36 (72)
Death	14 (28)
Refferal	
Yes	13 (26)
No	37 (74)
Asphyxia	
Severe asphyxia	18 (36)
Moderate asphyxia	32 (64)

Table 2: Morbidity found in this study group

Variables	N = 50
Hypothermia	
Yes	14 (28)
No	36 (72)
Respiratory distress syndrome	
Yes	39 (78)
No	11 (22)
Neonatal seizure	
Yes	4 (8)

No	46 (92)
Hypoglycemia	
Yes	33 (86)
No	17 (14)

Table 1 showed the subjects dominated by male (58%) with gestational age < 37 week or premature (72%), weight for gestational age is small gestational age (78%), birth weight <2500 gram (44%), lower ANC (82%), and 32 subject (64%) with moderate asphyxia. There was 34 (68%) mother age, >35 years old and higher mother education (82%). In this study found that mostly the mother was sectio-caesaria delivery (64%), there is no preeclampsia (70%), there is no premature rupture of membrane (82%), there is no antepartum bleeding (90%) and referral (74%).

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4. Discussion

Birth asphyxia remains one of the top ten conditions responsible for neonatal death in Indonesia and is recognized as an important cause of morbidity among newborns.⁴ According to WHO, 4 to 9 million newborn develop birth asphyxia each year and at least the same number develop severe consequences such as epilepsy, cerebral palsy, and developmental delay. Neurological complications in survivor impose tremendous medical and financial burdens that affirm the importance of taking swift steps to prevent birth asphyxia.³

Biological mechanisms have been suggested to explain this male disadvantage phenomenon.¹³ The explanation could involve a transient cerebral anoxia and death of respiratory control neurons in the brainstem that could prevent emergency resuscitation or auto resuscitation in males.¹⁷ A study suggested that the Y chromosome does not harm; the female protection at the times of cerebral anoxia is rather related to the presence of an additional X chromosome. Therefore, females are more resistant to hypoxia than males. In our study we found that neonatal asphyxia was predominantly in male (58%). This finding is similar with several studies such as MA Mohamed et al¹⁷ (56, 1%) and Kardana¹⁵ (57, 1%) and Jodjana et al (75, 6%).⁵³

Causes of perinatal birth asphyxia may be prenatal, intranatal and postnatal. Risk factors from prenatal includematernal age, non attendance for antenatal care, and preeclampsia.^{7, 8, 9} Advanced maternal age is significantly associated with adverse obstetrical outcomes as well as an increased of pregnancy-induced hypertension, gestational diabetes, antepartum hemorrhage and the need for Caesarian deliveries. Cesarean delivery was also tremendously increased in those mothers. On top of this, advanced maternal age pregnancy was also found to be a major risk factor for preterm delivery, low birth - weight, low fifth minute APGAR score and perinatal death.²¹ In our study shows that the neonatal asphyxia mostly in mother >35 years olds (68%). This finding is similar with the research conducted by Lamminpaa et al²² that advance maternal age

(12%) and Berglund et al⁴⁸ (18%) can increased neonatal asphyxia. This finding suggests that pregnancy and labour in all age groups should be effectively managed as maternal age cannot predict the occurrence of birth asphyxia.

Ante Natal Care (ANC) is comprehensive health supervision of a pregnant women. Quality of ANC assessed on the frequency and standard of ANC. During pregnancy care, women have the right to get counseling related to things that can endanger the mother and fetus during pregnancy.³⁷ To get extensive knowledge about pregnancy, women must be taught early to recognize the danger signs of pregnancy so they can prepare themselves when the time of delivery arrives when an emergency occurs.³¹ The components of ANC include: risk identification; prevention and management of pregnancy - related or concurrent diseases; and health education and health promotion.³⁷ In this study showed that the neonatal asphyxia were low ANC (82%). This finding was in line with the research conducted Yusnita (87%)³⁰ and Ganedkk (34%).⁴⁹

Preeclampsia is possible for asphyxia neonatorum. Preeclampsia can cause vasospasme which effect failure trofoblast insertion blood vessel muscular so it can damaged and obstruction blood flow in the placenta. This condition can cause hypoxia of the fetus.²³ In our study shows that the neonatal asphyxia were most no preeclampsia (70%). This finding is different with the research conducted by Kusumaningrum et al³⁴ (26, 8%), that preeclampsia can increase asphyxia neonatorum. The result is different caused by overall the subject of this research most none preeclampsia and many other factor can induced neonatal asphyxia such as prematurity, very low birth weight and prolong rupture of membran.

Risk factors from intranatal include prolonged rupture of membranes, antepartum bleeding, placenta previa, solution placenta, delivery with caesarian section, vaccum extraction.^{7, 8, 9} Prolonged rupture increases the possibility of infection. It causes more stress for the newborns. The most common complications of prolonged rupture of the membrane are amnionitis and endometritis. Both mother and the fetus are at a high risk of developing an overwhelming infection in the bloodstream (sepsis). In our study shows that the neonatal asphyxia were most none prolong rupture of membrane (82%). This finding is different with the research/ conducted by Aslam et al¹⁹ and Wiradharma et al⁵⁰ that prolonged rupture (33%) and (89%) can increase asphyxia neonatorum. The result is different caused by overall the subject of this research most none PROM and early antibiotic giving mother can prevent sepsis, so it can reduce neonatal asphyxia.

Anemia and shock are complication for antepartum bleeding because anemia can led to impaired function plasenta which as an O₂ and CO₂ circulation and a nutrient from the mother to fetus.²⁴ In the antepartum bleeding, there are decreased blood flow from mother to placenta so the hipoxemia can occur in the fetus. This condition can lead to perinatal asphyxia if the tranfusion to the mother or delivery is postpone.⁵¹ In our study showed different result, that in neonatal asphyxia didn't have antepartum bleeding (88%). This finding is different with the research Gilang et al²⁵ (81,

6%) and Utomo⁵² (5, 1%) that antepartum bleeding is increase asphyxia neonatorum. The result is different caused by the immediate treatment of complication antepartum bleeding with the termination of pregnancy and transfusion Packed Red Cell if there is anemia in pregnancy led to the asphyxia neonatorum rate to decline.

Section caesaria is one of the predisposition factor for asphyxia neonatorum. Compression of a fetal thorax at spontaneous labor encourages fluid to escape the airway higher than section caesaria and childbirth with section caesaria leads to asphyxia as a result of the use of analgesic and anaesthetic drugs, it can induce fetal respiratory depression.³⁵ In our study shows that the neonatal asphyxia were most section caesaria delivery (67%). This finding is was in line with the research conducted by Maya Safiti (70%)³⁶ and Utomo (61, 8%).⁵²

Risk factor from postnatal include low birth weight infants, prematurity, and Small for Gestational Age (SGA).^{7, 8, 9} Preterm baby delivery also emerged as one of the significant risk factor of birth asphyxia. It may due to the fact that preterm babies face multiple morbidities including organ system, immaturity specially lung immaturities causing respiratory failure.¹⁵ In our study showed that the neonatal asphyxia were most preterm (67%). This finding was in line with the research conducted by Purwaningsih et al²⁰ (82, 9%) and Aslam HM et al¹⁹ (53, 7%).

Infants born with LBW have little alveoli and the surfactants that covered the alveoli were also not produced much. Surfactant was a substance that prevent the occurrence of collapse during expiration. Lumen small respiratory system, collapse or airway obstruction, and immature lung blood vessels. This condition might interfere the baby's effort to breathe and often result in respiratory distress.¹⁷ In this study showed that the neonatal asphyxia were most LBW (67%). This finding was in line with the research conducted by Purwaningsih et al²⁰ (84, 3%) and Kardana¹⁶ (91, 4).

Small for gestational age (SGA) defined as birth weight 2 standard deviations below the mean weight for gestational age or below the 10th percentile for gestational age, has been associated with stillbirth and neonatal and postnatal mortality. Perinatal asphyxia during labor is the most serious potential complication. It is a risk if SGA caused by placental insufficiency because each uterine contraction slows or stops maternal placental perfusion by compressing the spiral arteries. This condition can cause hypoxia of the fetus.²⁶ In our study shows that the neonatal asphyxia were Small Gestational Age (78%). This finding is line with the research Jin Cheng et al²⁷ (72%).

Neonatal mortality is still a problem in Indonesia, especially in RSUP Sanglah Denpasar, Bali. The neonatal mortality rate in Sanglah Hospital in 2019 is 28.2%. neonates died with sepsis (67.57%), prematurity (9, 9%) severe asphyxia (5, 41%).⁴⁷ Perinatal asphyxia can result in profound systemic and neurologic sequelae due decreased blood flow and/or oxygen to a fetus or infant during the peripartum period.⁵ When placental (prenatal) or pulmonary (immediate post - natal) gas exchange is compromised or ceases altogether, there is partial (hypoxia) or complete (anoxia)

lack of oxygen to the vital organs.⁴³ This results in progressive hypoxemia and hypercapnia. If the hypoxemia is severe enough, the tissues and vital organs (muscle, liver, heart, and ultimately the brain) will develop an oxygen debt. Anaerobic glycolysis and lactic acidosis will result.⁶ However, continuous severe metabolic acidosis may eventually lead to vital organ and cerebral injury cascades, leading to neonatal hypoxic ischemic encephalopathy (HIE) or to death.⁵⁴ In our study we found the outcome asphyxia neonatorum were life (72%). This finding is different with the research conducted by Chowdury et al⁴⁴ that the proportional distribution of the major causes of neonatal deaths was asphyxia neonatorum (44%). This condition was different caused by immediately treatment for asphyxia neonatorum can reduce the neonatal mortality.

Poor prognostic factors like repeated seizures, APGAR score of ≤ 4 at 10 minutes or later, assisted ventilation for >24 hours, hypoglycemia, polycythemia, requirements of inotropes and hypothermia.⁸

Birth asphyxia and perinatal stress increase the risk of hyperinsulinism in the neonatal period because of the use of anaerobic metabolism to maintain blood glucose concentrations. During asphyxia, anaerobe glycolysis process results in the production of 2 molecules of adenosine triphosphate (ATP) from each molecule of glucose, instead of 38 ATP which usually were produced during aerobic condition. Anaerobic glycolysis elevates lactic acid production. Severe acidosis, on the other hand, diminishes glycolysis, causes loss of cardiovascular autoregulation, and decreases cardiac function. Furthermore, this process results in local ischemia and limitation in glucose transportation. The unexplained catecholamine release and hyperinsulinemia will decrease glycogen storage. Hypoxia of the brain increases glucose consumption. Moreover, combined hypoglycemia and asphyxia results in the failure of compensatory mechanism to save the brain from damage due to persistent hypoxia.³² In this research shows that there were hypoglycemia 86% in asphyxia neonatorum. This finding was in line with the research conducted Mufidati et al³⁹ that hypoglycemia (71%) as a comorbid factor for asphyxia neonatorum.

Respiratory distress is one of the most common problems presented within the first few days of life. Respiratory failure is a leading cause of neonatal mortality and is responsible for nearly 200 newborn deaths each year (1 in 1, 100 live births), including preterm newborns, representing 15% of total national neonatal mortality.⁴³ The infant with respiratory distress exhibits tachypnea, grunting, nasal flaring, and retractions of the chest wall, and may have cyanosis in room air.¹ Respiratory distress is that babies have an arterial oxygen tension (PaO₂) <50 mmHg and a requirement for supplemental oxygen to maintain PaO₂ >50 mm Hg, or a requirement for supplemental oxygen to maintain a pulse oximeter saturation $>85\%$. Respiratory disease may result from developmental abnormalities that occur before or after birth. More common caused respiratory diseases, such as Transient Tachypnea of the Newborn (TTN), Hyaline Membrane Disease (HMD), neonatal pneumonia, Meconium Aspiration Syndrome (MAS), and persistent pulmonary hypertension of the newborn (PPHN),

result from complications during the prenatal to postnatal transition period. Respiratory failure mechanisms in infants can be caused by hypoxia, ischemia, meconium aspiration, left ventricle dysfunction, coagulation system leaks, oxygen toxicity, and mechanical ventilation effects. In addition, a combination of pulmonary and systemic resistance can intensify the ratio of pulmonary and systemic resistance⁴⁰. In this research shows that there were respiratory distress (78%) in asphyxia neonatorum. This finding was in difference with the research conducted Parkash et al⁴³ and Solayman et al⁵⁵ found the proportion asphyxia neonatorum was lower in respiratory distress (10, 7%) and (7, 5%), in this research, the incident of respiratory distress were higher due to the removal of the data without any other cause of respiratory distress.

Neonatal seizure is a paroxysmal alteration caused by hypersynchronous discharge of a group of neurons.³⁸ Neonatal seizures are a danger sign or emergency that must be handled quickly in order to not increase mortality and morbidity. Causes of neonatal seizures are different, Hypoxic Ischemic Encephalopathy (HIE) is the leading cause of most neonatal seizures. HIE is a condition where there is a decrease in blood and oxygen levels to the brain. This HIE is a neurological complication of neonatal asphyxia.³³ In this research shows that there were no neonatal seizure (92%) in asphyxia neonatorum. This finding was different with the research conducted Thakkar et al⁴¹ that the neonatal seizure (62, 2%) was comorbidity factor for severe asphyxia neonatorum. In this study, the incidence neonatal seizure was low due to we included all degree of asphyxia.

The hypothermic asphyxiated neonates (birth temperature between 32°C and 36°C) were noted to have increased mortality (25%) compared with the 0% mortality in normothermic asphyxiated neonates (birth temperature of >36°C). Increased mortality in hypothermic neonates can be explained by the decreased metabolic activity and energy failure (decreased generation of ATPs) secondary to hypothermia. Another possibility is the decreased cardiac contractility associated with hypothermia, as shown in one animal model study, leading to decreased perfusion of the organs and causing multiorgan failure. Also, previous studies have shown increased incidence of complications in neonates with hypothermia.⁴² In this research shows that there were no hypothermia (72%) in asphyxia neonatorum. This finding was line with the research conducted Phoya et al⁵⁶ that hypothermia (11%) was low for comorbid present in asphyxiated neonates. This finding suggested that immediately resuscitation for the asphyxia neonatorum was by keeping the temperature body still warm, it can reduce the incident hypothermia in neonates.

5. Conclusion

The characteristic of neonatal asphyxia in our center are dominated by male, low birth weight, gestation age < 37 weeks, with caesaria delivery, small gestational age, mother with age > 35 years old and low quality of ANC. Our subjects also tend to characteristic comorbid factor of asphyxia which consists of a respiratory distress syndrome and hypoglycemia. The limitation of this study is that it uses

secondary data, namely patient medical records, so have risk bias information and inaccurate data. This study is not analyzing the relationship between profiles and outcomes so that they cannot describe the predictor factors. Further research is needed to look at the predictor factors affecting asphyxianeonatorum outcomes treated at the neonatal ward.

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