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Risk factors of severe perinatal asphyxia at tertiary hospital

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ABSTRACT

Background. Perinatal asphyxia is still one of the main causes of neonatal mortality and morbidity, especially in the first week of life in developing countries. In Indonesia, based on data reported by the Directorate of Family Health in 2020, of the 28,158 deaths of infants and toddlers, 72% (20,266 deaths) occurred during the neonatal period. One of the causes of neonatal death is perinatal asphyxia.

Objective. To analyze risk factors affecting severe perinatal asphyxia in tertiary hospital.

Method. Analytical observational research with case-control design. The data source is secondary data on mothers and babies born at Dr. Soetomo General Hospital from January 1 to December 31, 2021. The inclusion criteria were all neonates with perinatal asphyxia and the exclusion criteria were incomplete data.

Results. The prevalence of severe perinatal asphyxia at Dr. Soetomo General Hospital in 2021 is 3.9% (115/2,885). Prematurity was significantly associated with severe perinatal asphyxia (p=0.000). Low birth weight is also significantly related to severe perinatal asphyxia (p=0.000). The most dominant risk factor for severe perinatal asphyxia is prematurity. Extremely preterm have a 232.8 (95% CI: 35.8-2920.3) times higher risk of experiencing perinatal asphyxia compared to very preterm (OR 36.2, 95% CI: 12.4-105.4), moderately preterm (OR 11.6, 95 %CI: 4.1-22.6) and late preterm (OR 3.3, 95%CI: 1.1-9.1).

Conclusion. Risk factors for severe perinatal asphyxia are prematurity and low birth weight. Prematurity is the most dominant risk factor for severe perinatal asphyxia in tertiary hospital.

Keywords: perinatal asphyxia, risk factors

INTRODUCTION

Perinatal asphyxia is the failure of a newborn to initiate and maintain breathing immediately after birth which can result in decreased perfusion, ischemia, and organ failure [1]. Perinatal asphyxia is associated with several antepartum, intrapartum, and fatal risk factors [2]. Globally, perinatal asphyxia is still a problem. One of the main causes of neonatal mortality and morbidity, especially in the first week of life in developing countries. Perinatal asphyxia accounts for 28% of neonatal deaths every year throughout the world and around 29% of neonatal deaths in early life [3]. In Indonesia, based on data reported by the Directorate of Family Health in 2020, of 28,158 deaths of infants and toddlers, 72% (20,266 deaths) of which occurred during the neonatal period. The most common cause of neonatal death is low birth weight (LBW). Other causes of death include perinatal asphyxia, infection, congenital abnormalities, and neonatal tetanus [4].

OBJECTIVES

This study aims to identify and analyze intrapartum and fetal risk factors associated with the incidence of severe perinatal asphyxia at Dr. Soetomo Hospital, Surabaya.

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METHOD

Design

Analytical observational research with case-control design. The data source is secondary data on mothers and babies born at Dr. Soetomo General Hospital from January 1 to December 31, 2021.

Data collection

The data collection method was total sampling for case data that met the inclusion and exclusion criteria, while control data was obtained by simple random sampling to meet the ratio of cases and controls of 1:2. Intrapartum risk factors (malpresentation, premature rupture of membranes, meconium membranes, difficult labor and induction of labor) and fetal risk factors (prematurity, LBW, IUGR, and congenital abnormalities) are independent variables in this study. Meanwhile, severe perinatal asphyxia is the dependent variable.

Inclusion criteria

The case sample is a newborn who experienced severe perinatal asphyxia. The control sample was a newborn who experienced severe perinatal asphyxia.

Exclusion criteria

Neonates with incomplete data were excluded from the study.

Case definition of severe perinatal asphyxia

Perinatal asphyxia in this study was defined as gas exchange disorders characterized by one of the criteria, namely metabolic or mixed acidemia from umbilical cord blood (pH <7.0), or a persistent APGAR score of 0-3 at five minutes, or the presence of clinical neurological sequelae at immediate neonatal period and/or evidence of multi-organ system dysfunction according to The American Academy of Pediatrics.

Malpresentation is defined as the lowest part of the fetus, not the vertex, for example, forehead, face, shoulder, and buttock presentation.

Premature rupture of membranes is defined as spontaneous leakage of fluid from the amniotic sac before any signs of labor.

Meconium amniotic fluid is defined as amniotic fluid mixed with meconium. Meconium is the first feces that comes out when a new baby is born.

Difficult labor is defined as a condition when there are obstacles during the birthing process, for example, prolonged labor, labor dystocia, and the use of birth aids such as a vacuum.

Labor induction is defined as a method of initiating labor using oxytocin and misoprostol.

Prematurity is defined as birth that occurs at a gestational age of less than 37 weeks calculated from the first day of the last menstruation. Prematurity is divided into 4 types:

- Extremely Preterm is UG <28 weeks
- Very Preterm is UG 28-31 weeks
- Moderate Preterm is UG 32-33 weeks
- Late Preterm is UG 34-36 weeks

LBW (Low birth weight baby) is defined as a baby with a birth weight of less than 2500 grams.

- ELBW (Extremely Low Birth Weight) is birth weight <1000 grams
- VLBW (Very Low Birth Weight) is birth weight <1500
- LBW (Low Birth Weight) is birth weight <2500

IUGR (Intrauterine Growth Retardation) is defined as fetal size less than the 10th percentile of the baby's weight curve.

Congenital abnormalities are defined as abnormalities in body anatomy or body function abnormalities that occur at birth or while still in the womb.

Ethical issues

The study protocol was approved by the Institutional Ethics Committee of Dr. Soetomo General Hospital, Surabaya, Indonesia (No. 0986/LOE/304.4.2/VII/2022) on July 31, 2022.

Statistical analysis

This was performed with SPSS, version 20 (SPSS Inc, Chicago, Illinois, USA). Univariate analysis was carried out to examine the characteristics of each research variable. Bivariate analysis was carried out to look for the relationship between 2 variables, namely the independent variable (malpresentation, difficult or traumatic delivery, meconium membranes, premature rupture of membranes, labor induction, prematurity, LBW, IUGR, and congenital abnormalities) and the dependent variable (perinatal asphyxia). Multivariate logistic regression analysis was carried out to find the most dominant risk factors for perinatal asphyxia. Multivariate logistic regression analysis was carried out on variables that showed a significant p-value <0.05 in bivariate analysis to obtain an odds ratio (OR) value with a confidence interval (CI) of 95%. The results are significant if the OR value does not exceed one at the 95% CI.

RESULT

In this study from a total of 2,885 births in 2021, there were 115 cases of severe perinatal asphyxia with a prevalence of 3.9%. In this study, a total of 345 research subjects were obtained, consisting of 115 newborns with severe perinatal asphyxia and 230 newborns with non-perinatal asphyxia.

For the characteristics of the research subjects, the maternal condition for the perinatal asphyxia group showed that the high-risk age (<20 years and

>35 years) was 34.8% higher than the low-risk age of 32.6%. Multipara mothers were found to be higher at 34.3% than 31.2% for primipara in the case group. The highest maternal disease in the case group was pre-eclampsia at 38.6%. Other diseases found in each case group were anemia in 37.2%, eclampsia in 31.3%, antepartum hemorrhage in 26%, and Covid-19 infection in 12%. For the characteristics of the neonates condition, the male gender was 35.1% more dominant than the female gender 31.2% in the case group. The condition of premature babies, 41.8%, was also found to be more dominant than full-term babies, 5.2%, and post-term babies, 25% in the case group. Spontaneous labor at 35.4% was the most common type of labor among cesarean section deliveries at 33% and forceps extraction deliveries at 25% in the case group. Perinatal asphyxia cases also had a higher mortality rate of 94.1% compared to the control group of 5.9% (Table 1).

TABLE 1. Basic Characteristics of Subjects

Variable	Asphyxia (%) n=115	Non-Asphyxia (%) n=330
Maternal condition		
High risk age (<20 years dan >35 years)	40 (34.8)	75 (65.2)
Low risk age (21-35 years)	75 (32.6)	155 (67.4)
Primipara	35 (31.2)	77 (68.8)
Multipara	80 (34.3)	153 (65.7)
Anemia		
Yes	71 (37.2)	120 (62.8)
No	44 (28.6)	110 (71.4)
Pre-eclampsia		
Yes	34 (38.6)	54 (61.4)
No	81 (31.5)	176 (68.5)
Eclampsia		
Yes	5 (31.3)	11 (68.7)
No	110 (33.4)	219 (66.6)
Covid 19 Infection		
Yes	12 (12)	88 (88)
No	103 (42)	142 (58)
Antepartum hemorrhage		
Yes	6 (26)	17 (74)
No	109 (33.9)	213 (66.1)
Neonates condition		
Male	65 (35.1)	120 (64.9)
Female	50 (31.2)	110 (68.8)
Premature	110 (41.8)	153 (58.2)
Full term	4 (5.2)	74 (94.8)
Post Term	1 (25)	3 (75)
Type of labor		
Spontaneous	28 (35.4)	51 (64.6)
Forceps extraction	2 (25)	6 (75)
Caesarean section	85 (33)	173 (67)
Outcome		
Death	80 (94.1)	5 (5.9)
Survive	35 (13.5)	225 (86.5)

Regarding the characteristics of intrapartum risk factors, for the case group, the percentage of malpresentation was 29.5%, premature rupture of membranes was 44.3%, meconium membranes were 23.5%, difficult labor was 12.5% and labor induction was 66.7% (Table 2).

In terms of the characteristics of the fetal risk factors, prematurity was 41.8%, LBW was 44.7%, IUGR was 33.3% and congenital abnormalities were 30.8% in the case group. In terms of prematurity, the percentage of extremely preterm was 95%, very preterm 70.2%, moderate preterm 43%, and late preterm 17.6% in the case group. For LBW risk factors, the percentage for LBW was 35.8%, VLBW 60.8%, and ELBW 100% in the case group (Table 3).

TABLE 2. Characteristics of Intrapartum Risk Factors

Variable	Asphyxia (%) n=115	Non-Asphyxia (%) n=230
Malpresentation		
Yes	18 (29.5)	43 (70.5)
No	97 (34.2)	187 (65.8)
Premature rupture of membranes		
Yes	27 (44.3)	34 (55.7)
No	88 (31)	196 (69)
Meconium membranes		
Yes	4 (23.5)	13 (76.5)
No	111 (33.8)	217 (66.2)
Difficult labor		
Yes	1 (12.5)	7 (87.5)
No	114 (33.8)	223 (66.2)
Labor induction		
Yes	4 (66.7)	2 (33.3)
No	111 (32.7)	228 (67.3)

TABLE 3. Characteristics of Fetal Risk Factors

Variable	Asphyxia (%) n=115	Non-Asphyxia (%) n=230
Premature		
Yes	110 (41.8)	153 (58.2)
- Extremely preterm	21 (95)	1 (5)
- Very preterm	40 (70.2)	17 (29.8)
- Moderate preterm	28 (43)	37 (57)
- Late preterm	21 (17.6)	98 (82.4)
No	5 (6)	77 (94)
LBW		
Yes	109 (44.7)	135 (55.3)
- ELBW	ELBW	0 (0)
- VLBW	VLBW	20 (39.2)
- LBW	LBW	115 (64.2)
No	6 (6)	95 (94)
IUGR		
Yes	11 (33.3)	22 (66.7)
No	104 (33.3)	208 (66.7)
Congenital abnormality		
Yes	8 (30.8)	18 (69.2)
No	109 (34)	212 (66)

Bivariate Analysis

In this study, it was found that of the five intrapartum risk factor variables and four fetal risk factor variables, the only ones that had a statistically significant relationship with perinatal asphyxia were the fetal risk factors, namely prematurity and LBW with a p-value <0.05 with Pearson Chi-square. These two variables will then be analyzed using multivariate logistic regression analysis to look for more dominant risk factors (Table 4).

TABLE 4. Bivariate Analysis of Research Variables

Variable	Asphyxia (%) n=115	Non-Asphyxia (%) n=230	P
Malpresentation			
Yes	18 (29.5)	43 (70.5)	0.583[1]
No	97 (34.2)	187 (65.8)	
Premature rupture of membranes			
Yes	27 (44.3)	34 (55.7)	0.065[1]
No	88 (31)	196 (69)	
Meconium membranes			
Yes	4 (23.5)	13 (76.5)	0.538[1]
No	111 (33.8)	217 (66.2)	
Difficult labor			
Yes	1 (12.5)	7 (87.5)	0.277[2]
No	114 (33.8)	223 (66.2)	
Labor induction			
Yes	4 (66.7)	2 (33.3)	0.098[2]
No	111 (32.7)	228 (67.3)	
Premature			
Yes	110 (41.8)	153 (58.2)	
- Extremely preterm	21 (95)	1 (5)	
- Very preterm	40 (702)	17 (29.8)	0.000*[3]
- Moderate preterm	28 (43)	37 (57)	
- Late preterm	21 (17.6)	98 (82.4)	
No	5 (6)	77 (94)	
LBW			
Yes	109 (44.7)	135 (55.3)	
- ELBW	14 (100)	0 (0)	
- VLBW	31 (60.8)	20 (39.2)	0.000*[3]
- LBW	64 (35.8)	115 (64.2)	
No	6 (6)	95 (94)	
IUGR			
Yes	11 (33.3)	22 (66.7)	1.000[1]
No	104 (33.3)	208 (66.7)	
Congenital abnormality			
Yes	8 (30.8)	18 (69.2)	0.943[1]
No	109 (34)	212 (66)	

[1] Continuity correction, [2] Fisher's exact test, [3] Pearson chi-square

Multivariate logistic regression analysis

In this study, it was found that babies born extremely premature had a 232.8 times higher risk of experiencing perinatal asphyxia compared to other premature babies and full-term babies (CI 95%; 35.8-2920.3). Meanwhile, babies with LBW, based on multivariate logistic regression analysis, did not have a significant relationship with perinatal asphyxia.

TABLE 5. Multivariate Logistic Regression Analysis on Research Variables

Variable	Nilai *p*	OR	95% CI
Premature			
- Extremely Preterm	0,000	232.8	35.8-2920.3
- Very Preterm	0,000	36.2	12.4-105.4
- Moderate Preterm	0,000	11.6	4.1-22.6
- Late Preterm	0,022	3.3	1.1-9.1

DISCUSSION

Perinatal asphyxia is one of the causes of increasing morbidity and mortality rates in neonates. In this study, from 2,885 total births during 2021, 115 cases of severe perinatal asphyxia were found with a prevalence of 3.9%. This prevalence is the same as research in Nepal in 2019 at the Kathmandu Medical College Teaching Hospital, where the prevalence of perinatal asphyxia was found to be 3.66%. Other findings in research in Ethiopia in 2020 showed a higher prevalence in several hospitals, namely Nigist Eleni Mohammed Memorial Hospital (15.1%), Ayder Specialist Hospital in Tigray (18%), and Jimma Medical Center (18%) [5]. These differences could be due to differences in methodology and/or differences in research settings and differences in the services provided to pregnant women. Studies conducted in tertiary hospitals may show a higher incidence. This could be due to the majority of patients being referred to patients with more serious complications.

For risk factors for malpresentation, in this study based on bivariate analysis, it was found that they were not significantly related to the incidence of severe perinatal asphyxia (p=0.583). This is in contrast to research in Pakistan in 2012, which stated that births with a breech presentation would have a 2.96 times higher risk of experiencing perinatal asphyxia compared to births with other presentations (OR 2.96; CI95% 1.25-7.02, p= 0.01) [2]. In this study, malpresentation was not related to severe perinatal asphyxia, which could be due to choosing the right method of delivery to minimize the risk of severe perinatal asphyxia.

For risk factors for premature rupture of membranes, in this study based on bivariate analysis, it was found that they were not significantly related to the incidence of severe perinatal asphyxia (p=0.065). This finding is the same as research in Thailand in 2009, which stated that premature rupture of mem-

branes > 18 hours did not have a significant relationship to the incidence of perinatal asphyxia [6]. This is in contrast to research in Nepal in 2006, which stated premature rupture of membranes > 18 hours. significantly related to the mortality rate of perinatal asphyxia (RR: 1.83; 95% CI: 1.22–2.76) [7]. In this study, premature rupture of membranes was not associated with severe perinatal asphyxia, which could be due to good management of mothers with premature rupture of membranes, one of which is by treatment of infections and preparation for fetal maturation before birth.

For risk factors for meconium membranes, in this study based on the bivariate analysis, it was found that they were not significantly related to the incidence of severe perinatal asphyxia (p=0.538). This is in contrast to research in Ethiopia in 2018, which stated that amniotic meconium had a significant relationship with perinatal asphyxia. Meconium membranes have a 7.9 times higher risk of experiencing perinatal asphyxia [AOR=7.88; 95% CI (2.92-21.29)] [8]. In this study meconium was not associated with severe neonatal asphyxia, this could be due to early recognition of risk factors, and resuscitation management to evacuate the meconium at birth will reduce the risk of severe neonatal asphyxia in babies who are born.

For risk factors for difficult births, in this study based on bivariate analysis, it was found that they were not significantly related to the incidence of severe perinatal asphyxia (p=0.277). This finding is not the same with meta-analysis research in Ethiopia, stating that difficult labor has a 2.79 times higher risk of experiencing perinatal asphyxia (OR = 2.79, 95%CI=1.98-3.93), in addition to neonates born with instrumental assistance also had a 4.04 times higher risk of experiencing perinatal asphyxia compared to neonates born spontaneously (OR=4.04, 95%CI= 2.48-6.60) [9]. In this study, difficult births, namely births using instruments that are not related to perinatal asphyxia, can be caused by good birth assistance, appropriate resuscitation of the baby will be able to reduce the risk of severe perinatal asphyxia.

For risk factors for labor induction, in this study based on bivariate analysis, it was found that it was not significantly related to the incidence of severe perinatal asphyxia (p=0.098). This finding is in contrast to research conducted in Ethiopia in 2020, which stated that for mothers who gave birth using uterotonic drugs, newborns would have a 2.8 times higher risk of experiencing neonatal asphyxia [5]. In this study, labor induction was not related significantly to severe perinatal asphyxia can be caused by close observation of the condition of the fetus during induction which can reduce the risk of severe perinatal asphyxia.

In this study, after carrying out a multivariate logistic regression analysis, the results showed that prematurity was significantly associated with severe perinatal asphyxia, where extremely preterm prematurity had a 232.8 times higher risk of experiencing severe perinatal asphyxia compared to other types of prematurity and term babies. (CI 95%; 35.8-2920.3). This finding is the same with several studies, especially in developing countries, including research in Tigray, Ethiopia in 2018, which stated that premature babies had a 2.2 times risk of experiencing perinatal asphyxia. This research is in same as research conducted in Jordan which found that premature babies have a higher risk of asphyxia at birth. Premature babies are more susceptible to ischemia due to imperfect blood-brain barrier formation. Premature babies also face various diseases including organ system immaturity, especially lung immaturity which causes respiratory failure, and cardiopulmonary transition failure due to lack of surfactant which functions to maintain the respiratory system and tissue perfusion after birth. Premature babies are also vulnerable to comorbidities that will interfere with normal functioning in extrauterine life [8].

For risk factors for LBW, in this study, it was significantly associated with severe perinatal asphyxia based on bivariate analysis (p=0.000). After carrying out multivariate analysis, it was found that LBW was not the dominant risk factor for severe perinatal asphyxia. This is the same with research in Bangkok, Thailand in 2009, which stated that the risk of asphyxia for a fetus with a birth weight of less than 2,500 grams was 2.46 times greater than for a fetus with a birth weight of more than 2,500 grams [6]. Research in Tigray, Ethiopia in 2018, also stated that birth weight has a significant relationship to neonatal asphyxia. Low birth weight is 6.9 times more likely to experience neonatal asphyxia than normal weight (≥ 2500 g). Low birth weight (LBW) babies are often associated with maternal complications such as anemia, hypertension, and diabetes that exist in preconception or antepartum. To reduce the risk of LBW, pregnant women should be advised to carry out routine antenatal checks and stop or reduce risky activities that cause the fetus to experience LBW, for example, smoking or consuming alcohol [8].

For IUGR risk factors, in this study based on bivariate analysis, it was found that they were not significantly related to the incidence of severe perinatal asphyxia (p=1,000). This finding is similar to research in Thailand in 2009, which stated that IUGR did not have a significant relationship with perinatal asphyxia (p=0.72) [6]. IUGR is the second leading cause of perinatal death and is responsible for 30% of stillbirths, as well as being a cause of the most

common of premature birth and neonatal asphyxia [10]. Preventive interventions must be directed at women's health and nutrition as the most important cause of IUGR in developing countries [11]. In this study, IUGR was not related to perinatal asphyxia, which could be due to appropriate management of pregnancy maturation and resuscitation of the baby at birth which could minimize the risk of severe perinatal asphyxia.

For risk factors for congenital abnormalities, in this study based on bivariate analysis, it was found that they were not significantly related to the incidence of severe perinatal asphyxia (p=0.943). This finding is in contrast to research in Seoul, Korea in 2013 which stated that congenital abnormalities were a significant risk factor for the incidence of perinatal asphyxia in BBLSR babies [12]. In this study, congenital abnormalities not related to perinatal asphyxia could be caused by early detection of congenital abnormalities during pregnancy can anticipate preparations during delivery assistance to reduce the risk of severe perinatal asphyxia at birth.

CONCLUSION

We identified at least one risk factor associated with most cases of severe perinatal asphyxia, namely prematurity. In extremely preterm neonates, the risk of perinatal asphyxia will increase. Low birth weight is also related to prematurity, so the combination of the two will increase the risk of perinatal asphyxia.

In the absence of risk factors, the likelihood of perinatal asphyxia is very low. Perinatal asphyxia will be higher in tertiary hospitals because patients arrive with more severe conditions. Management of antepartum risk factors must also be improved at the basic health service level which will have a major impact on the condition of the fetus. Future research will address the question of whether a more integrated approach considering risk factors and new additional monitoring methods can improve awareness of fetal status and, consequently, prediction of asphyxia.

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