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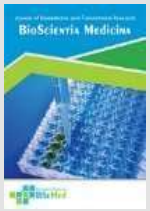

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Correlation Between APGAR Scores and the Incidence of Hyperbilirubinemia in Neonates at Wangaya Regional General Hospital, Denpasar

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A B S T R A C T

Background: Hyperbilirubinemia is defined as total serum bilirubin level at ≥ 5 mg/dl. In Indonesia, the prevalence of jaundice is 13,7-85%. One of the risk factors for hyperbilirubinemia in neonates is babies born with a history of asphyxia. The diagnosis of asphyxia can be enforced by the APGAR scoring system. This study aims to determine the relationship between APGAR values and the incidence of hyperbilirubinemia in neonates treated at Wangaya Regional General Hospital. **Methods:** This research is an analytic observational study using a cross-sectional approach, which was carried out in April-May 2022. The sample was taken by consecutive sampling. Bivariate analysis was performed using the chi-square test. Confounding variables will be controlled by design and by analysis. Influential risk factors were analyzed multivariate with logistic regression. Data were analyzed with SPSS software. **Results:** From 84 samples, 67, 9% had hyperbilirubinemia. The 1-minute APGAR score (P = 0,017, OR = 8,373, 95% CI; 1,468 – 47,738) and the 5-minute APGAR score (P = 0,034, OR =8,680, 95% CI; 1,172 – 64, 293) had significant correlation with the incidence of hyperbilirubinemia in neonates treated at Wangaya Regional General Hospital. **Conclusion**: Low APGAR scores have a significant correlation with the incidence of hyperbilirubinemia in neonates treated at Wangaya Regional General Hospital. The factor that most influences the incidence of hyperbilirubinemia is the 1-minute APGAR score. Neonates born with a low 1-minute APGAR score are 8,3 times at risk of experiencing hyperbilirubinemia.

1. Introduction

Hyperbilirubinemia is defined as a total serum bilirubin level at ≥ 5 mg/dl (86 µmol/L), portrayed by the yellowness of skin, conjunctiva, and mucosa. The prevalence of hyperbilirubinemia ranges between 60% in term babies and 80% in premature babies. In Indonesia, the prevalence of jaundice ranges from 13,7-85%.[1-3]

Hyperbilirubinemia can be considered as either a physiological or pathological condition that causes severe complications in the form of kernicterus. Kernicterus is a condition caused by high levels of indirect bilirubin that may occur if hyperbilirubinemia is not appropriately treated. The mortality rate for kernicterus is relatively high, around 10%, while the long-term morbidity is roughly 70%.[2]

One of the risk factors that may lead to hyperbilirubinemia in neonates is babies born with a history of asphyxia. According to the American College of Obstetrics and Gynecology (ACOG) and the American Academy of Pediatrics (AAP), asphyxia is a condition of disrupted blood gas exchange that causes progressive hypoxemia and hypercapnia with significant metabolic acidosis.[4] The diagnosis of asphyxia can be made by measuring the condition of the newborn baby using an APGAR scoring system, which is a simple method used to assess the general condition of a baby immediately after birth.[5] Based on

the background above, the author aims to assess the relationship between the APGAR score and the incidence of hyperbilirubinemia in neonates treated at the Wangaya Regional General Hospital, Denpasar.

2. Methods

This observational analytical study uses a cross-sectional approach to determine the relationship between APGAR scores and the incidence of hyperbilirubinemia in neonates treated at Wangaya Regional General Hospital, Denpasar. This research was carried out from April to May 2022. The subjects in this study were neonates born and treated at Wangaya Regional General Hospital in March 2021-March 2022 who met the inclusion and exclusion criteria. The sample inclusion criteria were neonates who were born and treated at Wangaya Regional General Hospital during March 2021-March 2022 and had complete medical records. Meanwhile, the exclusion criteria are hyperbilirubinemia diagnosed due to other causes (G6PD deficiency, ABO and rhesus incompatibility, polycythemia, TORCH), neonates with a history of maternal disease (hypertension, diabetes), neonates whose mothers suffer from tuberculosis, HIV/AIDS, hepatitis and syphilis, neonates experiencing neonatal sepsis, cephalhematoma, birth canal trauma, severe congenital abnormalities.

A consecutive sampling technique was used in this study. The data that has been collected will be processed using SPSS 26 for Windows software. Data analysis in the research was carried out bivariate with the chi-square test. Confounding variables are controlled by design by setting inclusion and exclusion criteria; hence, there are more constant variables. Confounding variables are also controlled by analysis; multivariate analysis is carried out so that the magnitude of their influence can be calculated and adjusted so that the pure impact of the independent variable on the dependent variable can be measured.

Multivariate analysis was carried out using the multiple logistic regression method. Bivariate analysis is carried out to test the relationship between two variables, and multivariate analysis is carried out to look at the relationship of several variables simultaneously to see whether these variables are related to each other. The variables analyzed in multivariate analysis are variables whose significance has previously been tested. If the p-value is <0.05, the variable can be meaningful and continued in multivariate analysis.

3. Results

This research was conducted in the Perinatology and NICU room at Wangaya Regional General Hospital in April-May 2022 by collecting secondary data from medical records. On March 2021-March 2022, there were 84 research samples that met the research inclusion and exclusion criteria. Sample characteristics can be seen in Table 1.

Table 1 shows that out of the 84 respondents, the majority were male (52.4%) with birth weight of ≥ 2500 grams (56.0%) and preterm gestational age (52.5%). The majority were also exclusively breastfed (63.1%) and were born by caesarean section or using instruments (59.5%). Respondents with a 1-minute APGAR score < 7 were (65.5%). For the 5th minute APGAR value, it was found that (52.4%) of respondents had an APGAR value < 7. The incidence of hyperbilirubinemia was found to be 67.9%.

In determining the relationship between the APGAR value and the incidence of hyperbilirubinemia, bivariate analysis was carried out using the chi-square test at a confidence level of 95% (p-value < 0.05) (Table 2). The results of the chi-square test in Table 2 show that there is a significant relationship between the 1-minute APGAR value (p = 0.000) and the 5-minute APGAR value (p = 0.000) with the incidence of hyperbilirubinemia.

Table 1. Basic characteristics of research subjects (n = 84).

Characteristics	Frequency (%)
Gender	
Male	44 (52,4%)
Female	40 (47,6%)
1 minute APGAR score	
APGAR score < 7	55 (65,5%)
APGAR score ≥ 7	29 (34,5%)
5-minute APGAR score	
APGAR score < 7	44 (52,4%)
APGAR score ≥ 7	40 (47,6%)
Birth weight	
< 2500 gram	37 (44,0%)
≥ 2500 gram	47 (56,0%)
Gestational age	
Preterm (< 37 weeks)	44 (52,4 %)
Full term (≥37 weeks)	40 (47,6 %)
Breastfeeding status	
No exclusive breastfeeding	31 (36,9%)
Exclusive breastfeeding	53 (63,1%)
Methods of childbirth	
Vaginal delivery	34 (40,5%)
Caesarean section or instrumental	50 (59,5 %)
Hyperbilirubinemia	
Yes	57 (67,9%)
No	27 (32,1%)
Total	84 (100%)

Table 2. Correlation between APGAR scores and the incidence of hyperbilirubinemia.

APGAR score		Hyperbilirubinemia		Total	p	PR	95% CI
		Yes	No				
1 minute APGAR score	< 7	49 (58,4%)	6 (7,1%)	55 (65,5%)	0,000	3.230	1,778-5,866
	≥ 7	8 (9,5%)	21 (25,0%)	29 (34,5%)			
5-minute APGAR score	< 7	42 (50,0%)	2 (2,4%)	44 (52,4%)	0,000	2.545	1,697-3,817
	≥ 7	15 (17,9%)	25 (29,7%)	40 (47,6%)			

The relative risk estimate in cross-sectional studies is expressed as a prevalence ratio (PR). From Table 2, it can be seen that neonates with a 1st minute APGAR value < 7 have a 3.23 times risk of experiencing hyperbilirubinemia (PR = 3.230; 95% CI = 1.778 – 5.866) compared to an APGAR value ≥ 7. Meanwhile, neonates with a minute APGAR value 5 < 7 have a 2.54 times risk of experiencing hyperbilirubinemia (PR = 2.545; 95% CI = 1.697 – 3.817) compared to an APGAR score ≥ 7.

Table 3. Correlation between birth weight, gestational age, breastfeeding status, delivery method, and the incidence of hyperbilirubinemia.

Category	Hyperbilirubinemia		Total	p	PR	95% CI
	Yes	No				
Birth weight						
< 2500 gram	32 (38,1%)	5 (5,9%)	37 (44,0%)	0,001	1.626	1,208-2,188
≥ 2500 gram	25 (29,8%)	22 (26,2%)	47 (56,0%)			
Gestational age						
Preterm	36 (42,9%)	8 (9,5%)	44 (52,4%)	0,004	1.558	1,125-2,159
Aterm	21 (25,0%)	19 (22,6%)	40 (47,6%)			
Breastfeeding status						
No exclusive breastfeeding	22 (26,2%)	9 (10,7%)	31 (36,9%)	0,641	1.075	0,799-1,446
Exclusive breastfeeding	35 (41,7%)	18 (21,4%)	53 (63,1%)			
Delivery method						
Vaginal delivery	22 (26,1%)	12 (14,3%)	34 (40,4%)	0,610	0.924	0,680-1,257
Caesarean section or instrumental	35 (41,7%)	15 (17,9%)	50 (59,6%)			

Before carrying out multivariate analysis, confounding variables in this study were also subjected to bivariate analysis using the chi-square test at a confidence level of 95% (p-value < 0.05) (Table 3). It was found that two factors had a significant relationship with the incidence of hyperbilirubinemia, including birth weight < 2500 grams (p = 0.001) (PR = 1.626; 95% CI = 1.208 – 2.188) and preterm gestational age (p = 0.004) (PR = 1.558; 95% CI= 1.125 – 2.159).

As for the factors that most influence the incidence of hyperbilirubinemia in neonates and the strength of the relationship, a multivariate analysis was carried out with a multiple logistic regression test on variables that had a significant relationship in the bivariate analysis, indicated by a p-value <0.05.

Table 4. Results of multivariate analysis with multiple logistic regression.

Category	B	Exp(B)	P	95% CI	
				Lower	Upper
1 minute APGAR score	2.125	8.373	0,017	1.468	47.738
5-minute APGAR score	2.161	8.680	0,034	1.172	64.293
Birth weight	1.146	3.147	0,150	0.660	14.999
Gestational age	1.644	5.147	0,032	1.151	23.262

According to Table 4 from the multivariate analysis, it was proven that the 1-minute APGAR value (p = 0,017) odd ratio is 8.373 and the 5-minute APGAR value (p = 0,034) odd ratio is 8.680; hence, a significant correlation with the incidence of hyperbilirubinemia in treated neonates at Wangaya Regional General Hospital. Meanwhile, the factor that most influences the incidence of hyperbilirubinemia in neonates treated at Wangaya Regional General Hospital is the 1-minute APGAR value.

4. Discussion

The results showed that of the 84 respondents, 57 people (67.9%) experienced hyperbilirubinemia, and 27 people (32.1%) did not experience hyperbilirubinemia. Based on the results of bivariate analysis, it is shown that there is a significant relationship between the 1-minute APGAR value and the incidence of hyperbilirubinemia in neonates treated at Wangaya Regional General Hospital (p = 0.000) and the prevalence ratio = 3.230, which means the risk of hyperbilirubinemia is 3.230 times in

neonates with the 1-minute APGAR value <7. This result is in accordance with several studies that have been conducted previously.

Latama et al. (2014) prove a significant relationship exists between the 1-minute APGAR score of 4-6 and 0-3 with the incidence of physiological neonatal jaundice (p=0.001) and the prevalence ratio = 1.695. It can be concluded that babies born with low 1-minute APGAR scores are 2 times more likely to experience physiological neonatal jaundice compared to those born with average 1-minute APGAR scores.[6]

In this study, the 5-minute APGAR value from the results of the bivariate analysis showed a significant relationship with hyperbilirubinemia in neonates treated at Wangaya Regional General Hospital (p = 0.000) and the prevalence ratio = 2.545, which means that neonates with a 5-minute APGAR value <7 had a risk of incident hyperbilirubinemia was 2.545 times greater than neonates with average 5 minute APGAR scores. These results are in alignment with research conducted by Latama et al. (2014), which stated that there was a significant relationship between the 5-minute APGAR score of 4-6 with the incidence of physiological neonatal jaundice (p = 0.023) and prevalence ratio = 5.167.[6]

Research conducted by Bizuneh et al. (2020) stated that asphyxia has a significant relationship with the incidence of hyperbilirubinemia in neonates (p = 0.012) with an odd ratio = 2.88, which means that neonates with asphyxia have a risk of hyperbilirubinemia 2.88 times greater than neonates without asphyxia. Research by Melinda et al. (2021) also showed similar results (p = 0.002), which means there is a significant relationship between asphyxia and the incidence of hyperbilirubinemia in neonates. Likewise, research conducted by Arsansi et al. (2020) showed that (p = 0.013) asphyxia influenced the incidence of hyperbilirubinemia in neonates.[1,3,7]

An APGAR score <7 is declared as asphyxia in newborn neonates, which causes insufficient oxygen intake, resulting in perfusion disorders through various organs and multi-organ dysfunction, especially in the brain, lungs, and liver. Jaundice may result since asphyxia affects the conjugation of bilirubin in the liver. Asphyxia also causes hepatic hypoperfusion, resulting in disturbances in hepatocyte bilirubin uptake and metabolism. Neonatal asphyxia can inhibit the activity of uridine diphosphate glucuronyltransferase (UDPGT) in the liver, thereby increasing unconjugated bilirubin levels. The severity of hypoxemia in asphyxiated neonates harms the liver and other body organs.[7-10]

Asphyxia will cause a redistribution of blood flow (diving reflex) to the brain, heart, and adrenal glands so that blood flow to other organs will be reduced; along with that, anaerobic metabolism occurs, which causes liver cell damage, which can lead to liver dysfunction.[4]

The occurrence of liver dysfunction may lead to hepatic-hypoxic injury and perinatal asphyxia with hypoxic-ischemic encephalopathy, resulting in an increase in various liver enzymes: aspartate transaminase (AST), alanine transaminase (ALT), alkaline phosphatase (ALP), lactate dehydrogenase (LDH) and total serum bilirubin (TSB). Hence, a correlation is found between liver dysfunction and the severity level of hypoxia.[7,9,11]

In this study, based on the results of bivariate analysis, a significant correlation was also found between birth weight and the incidence of hyperbilirubinemia in neonates (p=0.001) and prevalence ratio = 1.626. The number indicates the risk of hyperbilirubinemia in neonates was 1.626 times in neonates with a birth weight < 2500 grams. These results follow cross-sectional research conducted by Yasadipura et al. (2020), who stated that low birth weight (LBW) has a significant relationship with the incidence of hyperbilirubinemia (p = 0.042) and the prevalence ratio is 2,13 times more risky in neonates with LBW.[12]

Gestational age also had a significant relationship with the incidence of hyperbilirubinemia in this study; from the results of a bivariate analysis, it was found (p=0.004) a prevalence ratio of 1.558, which means the risk of hyperbilirubinemia increased by 1.558 times more significant in preterm neonates (< 37 weeks).

These results align with the research conducted by Arsandi et al. (2020), where an important relationship was found between the incidence of hyperbilirubinemia and gestational age (p = 0.000). Research conducted by Devi et al. also stated the same thing (p < 0.0001) that babies born at premature gestational age tend to experience hyperbilirubinemia.[13]

However, the bivariate analysis results of this study did not show a significant relationship between the incidence of hyperbilirubinemia and the delivery method in neonates treated at Wangaya Regional General Hospital (p = 0.610). The same results were also reported by Melinda et al. (2021) (p = 0.110) and Faiqah (2014) (p = 0.562). Thus, there was no significant relationship between the delivery method and the incidence of hyperbilirubinemia in neonates.[3,14]

In this study's bivariate analysis, breastfeeding status was not considered a significant factor correlated with the incidence of hyperbilirubinemia (p = 0,641). The same results were shown in research conducted by Scrafford et al. (2013) in Nepal, which stated that breastfeeding is not a risk factor for hyperbilirubinemia.[15]

Through this study, several factors were associated with the incidence of hyperbilirubinemia in neonates, including APGAR values at 1 and 5 minutes, birth weight, and gestational age. Then, these factors were carried out in a multivariate analysis using the logistic regression method; it was obtained that the 1-minute APGAR value (p = 0.017), odd ratio = 8.373, and the 5th-minute APGAR value (p = 0.034) with the odd ratio = 8.680 had a significant relationship with the incidence of hyperbilirubinemia in neonates treated at Wangaya Regional General Hospital, Denpasar. The factor that most influences the incidence of hyperbilirubinemia in neonates treated at Wangaya Regional General Hospital, Denpasar, is the 1st minute APGAR value.

The weakness of this research is the small sample size due to the reasonably short sample collection time, so further research is needed using a more significant number of samples over a longer time to confirm the results of the research that has been carried out.

5. Conclusion

Based on the research data, low APGAR scores result in a significant relationship with the incidence of hyperbilirubinemia in neonates treated at Wangaya Regional General Hospital, Denpasar. Many factors may influence the incidence of hyperbilirubinemia in neonates treated at Wangaya Regional General Hospital, Denpasar, but the 1-minute APGAR value is the most influential. Neonates born with a low 1-minute APGAR score are 8.3 times more likely to experience hyperbilirubinemia compared to neonates with a good APGAR score or ≥ 7.

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