



Relationship between birth weight and gestational age with the incidence of neonatal hyperbilirubinemia

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ABSTRACT

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Hyperbilirubinemia ranks fifth among causes of neonatal morbidity in Indonesia, with most babies born under 35 weeks of gestation and with low birth weight (LBW). Untreated hyperbilirubinemia can lead to kernicterus and neurological disorders. This study aimed to determine the relationship between birth weight and gestational age with hyperbilirubinemia. This study used a cross-sectional approach. Secondary data were collected from 50 infants using total sampling from 50 infants at Denpasar Women's and Children's Hospital (RSIA) during January-December 2024. Data were analyzed univariately using descriptive analysis and bivariate using the Spearman rank test because the data were not normally distributed. The results show that there was a relationship between birth weight and hyperbilirubinemia ($p < 0.001$), ($r = -0.727$). There was a relationship between gestational age and hyperbilirubinemia ($p < 0.001$) ($r = -0.857$). Midwives need to strengthen collaboration with pediatricians in monitoring bilirubin levels, especially in low-birth-weight and premature infants. In addition, parental education on adequate breastfeeding (8–12 times/day) is essential to promote bilirubin excretion.

INTRODUCTION

Maternal and child health remains a fundamental indicator of national health system performance and sustainable development. Despite global progress, neonatal mortality continues to contribute substantially to under-five mortality, particularly in low- and middle-income countries. According to the World Health Organization, approximately 2.3 million neonatal deaths occur annually, with the majority taking place within the first week of life. The leading causes include prematurity, low birth weight (LBW), and intrapartum-related complications, which together account for more than 60% of neonatal deaths^{1,2}. These findings highlight the persistent role of perinatal factors in neonatal morbidity and mortality.

Low birth weight, defined as a birth weight of less than 2.500 grams regardless of gestational age, remains a major global health concern. The global prevalence of LBW is estimated at 14–20%, with nearly 90–95% of cases occurring in developing countries^{2,3}. In Indonesia, national survey data indicate that the prevalence of LBW remains high, contributing significantly to neonatal mortality. Regional data from Bali Province also demonstrate a substantial burden of LBW cases, reflecting



ongoing challenges in maternal and neonatal health services. However, LBW is a heterogeneous condition, encompassing both preterm infants and term infants with intrauterine growth restriction (IUGR), which may differ significantly in physiological maturity and clinical outcomes.

One of the most common early complications associated with LBW and prematurity is neonatal hyperbilirubinemia. This condition arises from an imbalance between bilirubin production and elimination, primarily due to immature hepatic function. Neonatal hyperbilirubinemia is clinically characterized by elevated serum bilirubin levels and visible jaundice, typically appearing within the first week of life. It is estimated that approximately 60% of term neonates and up to 80% of preterm neonates develop some degree of hyperbilirubinemia^{4,5}. Although often physiological, a significant proportion may progress to severe hyperbilirubinemia if not properly managed.

From a pathophysiological perspective, preterm infants are particularly vulnerable due to reduced activity of hepatic uridine diphosphate glucuronosyltransferase (UGT1A1), decreased albumin-binding capacity, and increased enterohepatic circulation. These mechanisms lead to accumulation of unconjugated bilirubin and an increased risk of bilirubin-induced neurotoxicity^{6,7}. Severe hyperbilirubinemia can result in acute bilirubin encephalopathy and kernicterus, conditions associated with permanent neurological damage, including hearing loss, cerebral palsy, and developmental delay⁸. Although kernicterus is relatively rare in high-income settings, its incidence remains higher in resource-limited regions, emphasizing the need for early identification of risk factors.

Several studies have demonstrated a significant association between LBW and hyperbilirubinemia, as well as between prematurity and increased bilirubin levels^{7,9}. However, emerging evidence suggests that gestational age may be a stronger determinant of hyperbilirubinemia than birth weight alone, as it more accurately reflects hepatic maturity and metabolic capacity^{7,10}. Despite this, many studies continue to analyze these variables separately without adequately comparing their relative contributions or controlling for overlapping effects between prematurity and fetal growth restriction.

In addition, most available studies are conducted in large tertiary hospitals or developed countries, limiting their generalizability to local healthcare settings. In Indonesia, particularly at the facility level, data examining the combined relationship between birth weight, gestational age, and neonatal hyperbilirubinemia remain limited. This represents an important research gap, especially considering variations in population characteristics, clinical practices, and resource availability.

Data from RSIA Denpasar Women's Hospital indicate that the incidence of neonatal hyperbilirubinemia in the neonatal intensive care unit (NICU) remains relatively high and fluctuates annually, with 550 cases in 2022, 580 cases in 2023, and 567 cases in 2024. Preliminary data from January to June 2025 also reported 366 cases. These trends underscore the ongoing burden of hyperbilirubinemia and the need for evidence-based strategies to identify high-risk neonates. Therefore, this study aims to analyze the relationship between birth weight and gestational age with the incidence of neonatal hyperbilirubinemia. Understanding the relative contribution of these factors is essential to improve early detection, risk stratification, and targeted management of hyperbilirubinemia, particularly in high-risk neonatal populations.

METHODS

This was a correlational analytical study with a cross-sectional design. The aim was to analyze the relationship between birth weight and gestational age and the incidence of hyperbilirubinemia in neonates. The study was conducted at the Denpasar Women's Hospital (RSIA) in November 2025 using secondary data. The study population consisted of all newborns registered in the birth register and electronic medical records of the Denpasar Women's Hospital (RSIA) during January–December 2024. A sample of 50 neonates was selected using a nonprobability sampling technique with a total sampling method, including all neonates who met the inclusion criteria. The inclusion criteria included spontaneous birth and neonatal age greater than 24 hours. Gestational age was defined as the duration of pregnancy calculated from the first day of the last menstrual period or based on obstetric assessment and was recorded in completed weeks (preterm: <37 weeks; term: 37–42 weeks; post-term: >42 weeks), and birth weight defined as the neonate's body weight measured immediately after birth and recorded in grams in the medical record (Low Birth Weight (LBW): < 2500 grams and Normal Birth Weight: ≥

2500 grams). Neonates with incomplete medical records and those with previously known hemolytic disease were excluded from the study.

Data were collected through a search of medical records and electronic registers of the delivery room and intensive care unit of the Denpasar Women's Hospital (RSIA) using a secondary data checklist compiled based on the study variables. The independent variables in this study were birth weight and gestational age, while the dependent variable was the incidence of hyperbilirubinemia. The collected data were edited, entered, and tabulated, then analyzed using statistical software. Univariate analysis was used to describe the characteristics of each variable, while bivariate analysis was performed using the Spearman's rank correlation test because the data were not normally distributed. The significance level was set at $p < 0.05$.

This study has obtained ethical approval from the Research Ethics Committee of the Denpasar Ministry of Health Polytechnic (No. DP.04.02/F.XXIV.25/931/2025) and research permit from the Denpasar Women's Hospital (RSIA). All data were kept confidential in accordance with research ethics principles, including respect for persons, beneficence, and justice.

RESULTS AND DISCUSSION

Characteristics of Research Subjects

Table 1. Characteristics of respondents (n=50)

Characteristics	Total	
	f	%
Sex		
Female	29	58.0
Male	21	42.0
Total	50	100.0

A total of 50 neonates were studied. The majority of neonates with hyperbilirubinemia were female (58%), while 42% were male. These findings indicate a relatively balanced gender distribution, with a higher prevalence in female neonates.

This finding differs from several previous studies reporting a higher prevalence in male neonates due to genetic predispositions such as Gilbert's syndrome and G6PD deficiency, which are more common in males ¹¹. These differences may be influenced by variations in population characteristics, sample size, and environmental or healthcare-related factors.

Data Normality Test

Table 2. Normality test results

Variables	Kolmogorov- Smirnov ^b	
	n	sig.
Baby Birth Weight	50	0.01
Gestational Age	50	0.00
Bilirubin Levels	50	0.00

The Kolmogorov–Smirnov test showed that all variables had a significance value of less than 0.05, indicating that the data were not normally distributed. This non-normal distribution may be attributed to the relatively small sample size and variability in gestational age and birth weight. Therefore, non-parametric analysis using the Spearman Rank correlation test was applied to examine the relationship between variables.

Distribution of Birth Weight, Gestational Age, and Bilirubin Levels

Table 3. Birth weight, gestational age, bilirubin level (n=50)

Variables	n	Min	Max	Median	Mode	Average	Standard Deviation
BW	50	2025	3860	2400	2100	2582.28	562.440
GA	50	29	41	32	30	33.76	4.138
Bilirubin Levels	50	6.03	24.30	17.21	20.30	15.40	5.746

The univariate analysis showed that birth weight ranged from 2025 to 3860 grams, with a median of 2400 grams. Gestational age ranged from 29 to 41 weeks, with a median of 32 weeks. Total bilirubin levels ranged from 6.03 to 24.30 mg/dL, with a median of 17.21 mg/dL. These findings indicate that a considerable proportion of neonates in this study were classified as low birth weight and preterm, conditions that are strongly associated with elevated bilirubin levels.

Relationship between Birth Weight, Gestational Age, and Hyperbilirubinemia

Table 4. Spearman rank correlation between birth weight, gestational age, and hyperbilirubinemia (n=50)

Variables	r	p-value
Birth Weight and Hyperbilirubinemia	-0.727**	0.000
Gestational Age and Hyperbilirubinemia	-0.857**	0.000

The Spearman Rank analysis showed that both birth weight and gestational age were significantly associated with neonatal hyperbilirubinemia ($p < 0.05$). Birth weight demonstrated a strong negative correlation ($r = -0.727$), while gestational age showed a very strong negative correlation ($r = -0.857$). These findings indicate that lower birth weight and lower gestational age are associated with higher bilirubin levels in neonates.

Low birth weight (LBW) neonates were found to have a higher risk of hyperbilirubinemia. This is primarily due to immature hepatic function, particularly the reduced capacity for bilirubin conjugation. Hepatocellular immaturity limits the activity of bilirubin-processing enzymes, leading to inefficient conversion of unconjugated bilirubin into conjugated bilirubin¹². Previous studies consistently report that LBW infants exhibit decreased hepatic clearance, reduced enzymatic activity, and impaired biliary excretion, all of which contribute to bilirubin accumulation^{6,11}.

However, gestational age demonstrates a stronger and more direct association with hyperbilirubinemia than birth weight. This is because gestational age reflects the degree of developmental and functional maturity of vital organs, especially the liver. In preterm neonates, hepatic immaturity is characterized by significantly decreased activity of uridine diphosphate glucuronosyltransferase (UGT1A1), the key enzyme responsible for bilirubin conjugation¹². The reduced expression of this enzyme delays bilirubin clearance and results in elevated levels of unconjugated bilirubin.

Additionally, premature infants have lower serum albumin concentrations and diminished bilirubin-binding capacity. Albumin is essential for transporting unconjugated bilirubin in plasma; therefore, reduced albumin levels increase the proportion of free bilirubin, which is capable of crossing the blood–brain barrier and causing neurotoxicity¹⁰. This mechanism explains the higher susceptibility of preterm infants to bilirubin-induced neurological dysfunction (BIND) and kernicterus.

The enterohepatic circulation is also more active in premature neonates due to delayed intestinal motility and reduced gut microbiota activity. This leads to increased deconjugation of bilirubin by intestinal β -glucuronidase and reabsorption into the bloodstream, further elevating serum bilirubin levels¹³. Moreover, reduced expression of hepatic ligandin and decreased hepatic uptake capacity further impair bilirubin metabolism in preterm infants⁶.

Prematurity is also frequently associated with systemic conditions such as hypoxia, acidosis, and sepsis, which exacerbate bilirubin toxicity by disrupting albumin binding and increasing free bilirubin levels. Ikatan Dokter Anak Indonesia also emphasizes that these comorbid conditions significantly elevate the risk of severe hyperbilirubinemia and neurological complications. Importantly, while LBW can result from either prematurity or intrauterine growth restriction (IUGR), not all LBW infants exhibit the same degree of hepatic immaturity. Term infants with IUGR may have relatively more mature liver enzyme systems compared to preterm infants of similar weight. Therefore, gestational age serves as a more accurate predictor of bilirubin metabolism capacity than birth weight alone.

The median bilirubin levels observed in this study indicate clinically significant hyperbilirubinemia. This condition arises from an imbalance between bilirubin production and elimination, particularly in neonates with immature hepatic systems¹⁴. Reduced hepatic blood flow, impaired uptake, and decreased enzymatic conjugation further contribute to bilirubin accumulation¹⁰. These findings highlight the importance of early detection and management of hyperbilirubinemia, especially in premature neonates. Interventions such as phototherapy, early feeding, and close monitoring have been proven to reduce bilirubin levels and prevent complications¹⁵.

CONCLUSION

This study demonstrates that there is a significant relationship between birth weight and gestational age with the incidence of neonatal hyperbilirubinemia at RSIA Denpasar Women's Hospital. Both variables show a negative correlation, indicating that lower birth weight and lower gestational age are associated with higher bilirubin levels in neonates.

Importantly, gestational age exhibits a stronger correlation compared to birth weight, suggesting that the degree of physiological maturity - particularly hepatic function - plays a more dominant role in the development of hyperbilirubinemia. This finding confirms that prematurity is a critical determinant in impaired bilirubin metabolism and increased risk of bilirubin accumulation.

These results emphasize the need for early identification and close monitoring of neonates with low birth weight and especially those born preterm, as they represent high-risk groups for developing hyperbilirubinemia. Strengthening early screening, optimizing neonatal care, and ensuring adequate feeding practices are essential to prevent complications such as bilirubin-induced neurotoxicity.

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CONFLICT OF INTEREST

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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DECLARATION OF ARTIFICIAL INTELLIGENCE USE

The authors used ChatGPT (OpenAI, version GPT-5) to assist in improving the language and grammar of the manuscript. The authors reviewed and verified the content to ensure accuracy and integrity.

AUTHOR CONTRIBUTIONS

MCA conceptualized the study, performed the experiments, and wrote the original draft of the manuscript. GAT, NMDP and NPWR supervised the research, reviewed the methodology, and edited the final manuscript. All authors contributed to the article and approved the submitted version.

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