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Description of Risk Factors Affecting Neonatal Jaundice

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ABSTRACT

Background: Bilirubin is a chemical compound that is a product of catabolism by biliverdin reductase. Bilirubin is a yellow pigment compound. Increased bilirubin levels in babies' blood will cause neonatal jaundice and changes in skin and sclera color in babies. This study aims to determine the risk factors that influence neonatal jaundice
Methods: This research used correlational analytical observational research with a cross-sectional design, using medical records of birth and jaundice babies at Gatot Subroto Army Hospital, Hermina Depok Hospital, and Hermina Kemayoran Hospital in the period January 2023 - June 2023. The total sample was 300 samples. The research instruments and materials used in this study were medical records of babies experiencing jaundice at Gatot Subroto Army Hospital, Hermina Depok Hospital, and Hermina Kemayoran Hospital.
Results: Based on data analysis of several factors that have the potential to have a relationship with Neonatal Jaundice, namely: gender, type of delivery, birth weight, consumption of breast milk/formula milk, and gestational age, the results of data analysis were obtained using chi-square where for the gender factor the value was obtained. p_value 0.000 < 0.005, meaning that there is a significant relationship between gender and neonatal jaundice; for the type of delivery factor, the p-value was 0.188 < 0.005, meaning that there was no significant relationship between the type of delivery and the incidence of Neonatal Jaundice; For the birth weight factor, data was obtained with a p-value of 0.118 > 0.005, meaning that there was no significant relationship between birth weight and neonatal jaundice; Factors of consumption of breast milk/milk//formula milk on neonatal jaundice; Furthermore, the maternal gestational age factor has a p-value of 0.494>0.005, meaning that there is no significant relationship between the maternal gestational age factor and neonatal jaundice.
Conclusions: Of the six factors studied, two factors have a significant relationship to neonatal jaundice, namely gender and consumption of breast milk/formula milk

Keywords: Bilirubin, Neonatal Jaundice, Risk Factors

INTRODUCTION

Neonatal jaundice is a condition often experienced by neonates. Neonatal jaundice is a clinical condition in infants characterized by jaundice on the skin and sclera due to excessive accumulation of unconjugated bilirubin. Jaundice or jaundice will clinically appear in newborn babies if the blood bilirubin level is 5-7 g/dL. According to the World Health Organization (WHO) quoted from an article by Sukadi N (2021) and Dorji,

et al. (2023), most of 6.6 million babies died from neonatal jaundice in 2013 worldwide. Neonatal jaundice affects half of term newborns and 80% of premature newborns on a global scale. The incidence of neonatal jaundice in Southeast Asia is relatively high, ranking second globally with a figure of 251.3 per 10,000 live births. In 2014, as many as 73% of babies worldwide died within seven days of life due to jaundice making it the second leading cause of neonatal mortality. seventh globally [1,2].

According to Central Statistics Agency data for 2023, the Infant Mortality Rate (IMR) in Indonesia is 16.85 per 1,000 live births. Causes of neonatal disability and/or death include asphyxia, jaundice, hypothermia, neonatal jaundice, infection or sepsis, birth trauma, respiratory distress syndrome, and LBW congenital abnormalities (birth weight < 2500 grams) [3]. According to data from Basic Health Research 2007, quoted from an article by Gowen CW, et al (2018), regarding the causes of neonatal death, it shows that jaundice is the 5th cause of neonatal morbidity (5.6%) after respiratory disorders, prematurity, sepsis, and hypothermia. At Santa Elisabeth Batam Hospital, 22.8% of babies were born with hyperbilirubinemia [4].

The impact of increasing bilirubin levels in the blood can cause neurological disorders and even brain damage. Danger signs from increased levels of bilirubin in the blood in babies include lethargic symptoms, hypotonia, poor sucking reflexes, damage to the baby's brain cells, babies experiencing seizures (1.12%), kernicterus (1.3%), hepatic cirrhosis and the most common death. in neonates (13%). Several causes can cause neonatal jaundice in the first life of a newborn baby, namely lack of adequate breast milk intake for the baby, asphyxia or respiratory problems caused by lack of oxygen levels in the body, lack of body nutrition, and Low Birth Weight (LBW). and Premature Babies (BKB) or what many people know as premature babies [6,7]. Hemolysis such as ABO and rhesus incompatibility and G6PD enzyme deficiency can cause neonatal jaundice. Decreased bilirubin conjugation in the liver such as congenital hypothyroidism. Decreased bilirubin excretion (cystic fibrosis and bile duct abnormalities such as biliary atresia) can also cause neonatal jaundice. Causes such as damage to helper cells due to infection can also cause neonatal jaundice [8].

Risk factors for neonatal jaundice can be divided into 3 factors, namely the occurrence of complications during pregnancy, maternal including race, and breast milk. Perinatal factors that cause neonatal jaundice include infections caused by bacteria, viruses or protozoa, and postnatal trauma. Meanwhile, the neonatal factors themselves include prematurity, genetics, drug consumption, hypoglycemia, hypoalbuminemia, and low adequacy of breastfeeding. Another factor states that LBW babies have a greater risk of developing neonatal jaundice compared to babies born with normal weight [9,16]. This is one of the factors because the maturity of the baby's organs is not yet optimal. One of them is the maturity of the liver's functional processes to process erythrocytes which can lead to neonatal jaundice in babies at the beginning of their life after birth. When a new baby is born, it cannot function properly in carrying out its duties. The cause of babies turning yellow is due to the remainder of the breakdown of erythrocytes called bilirubin [10,11]. The increasing amount of bilirubin levels in the baby's body causes changes in the color of the skin and sclera in the baby. Jaundice can be seen in newborn babies who have blood bilirubin levels of around 5-7 mg/dL clinically. Meanwhile, the ultimate normal level of bilirubin in newborn babies is more than 10 mg/dL [12,13].

Neonatal jaundice therapy is by phototherapy and exchange transfusion. If the total serum bilirubin level does not decrease or continues to increase, then evaluate whether the intensity of the phototherapy lamp is sufficient (30μW/cm2/nm). Efforts to determine whether the baby needs phototherapy or exchange transfusion, then the bilirubin level plotted on the normogram

is total serum bilirubin. Phototherapy is performed in conditions where the direct bilirubin level is 50% or more of the total bilirubin. If the total serum bilirubin level is 25mg/dL or higher at any time, this condition is an emergency and the baby must receive intensive phototherapy treatment [5,14,15]

The most important stage in the management of jaundice in infants is determining the primary cause. The choice of therapy greatly determines the reduction in bilirubin levels (indirect bilirubin) including phototherapy, exchange transfusion, enzyme induction, and interruption of enterohepatic circulation, so the author is interested in researching factors associated with neonatal jaundice.

Based on the description of the background above, researchers are interested in conducting research that will be carried out with the title Risk Factors Associated with Neonatal Jaundice.

MATERIALS & METHODS

Research Design

This research is a correlational analytic observational study with a cross-sectional design, to determine the factors associated with neonatal icterus in infants where researchers conduct research or observations by measuring the independent variable and the dependent variable at the same time. This study was conducted to determine factors associated with neonatal jaundice.

Place and Time of Research

Research Place

The research was conducted at Gatot Subroto Army Hospital, Hermina Hospital Depok, and Hermina Hospital Kemayoran.

Research Time

The research was conducted at Gatot Subroto Army Hospital, Hermina Depok Hospital, and Hermina Kemayoran Hospital in the period January 2023 - June 2023.

Research Population and Sample

Research Population

Population refers to all people, events or things that will be investigated by research. The population in this study were babies diagnosed with neonatal jaundice by the doctor in charge of babies at RSPAD Gatot Subroto, Hermina Hospital Depok, and Hermina Hospital Kemayoran.

Research Sample

The research sample is a portion or representative of the population that will be studied in this study. The samples used were 300 research samples taken from medical records and stated that the samples were diagnosed with neonatal jaundice.

Research Instruments and Materials

The research instruments and materials used in this study were medical records of babies experiencing jaundice at the Gatot Subroto Army Hospital, Hermina Depok Hospital, and Hermina Kemayoran Hospital.

Inclusion and Exclusion Criteria

Inclusion Criteria

The inclusion criteria in this study are:

1. Babies were born at Gatot Subroto Army Hospital, Hermina Depok Hospital, and Hermina Kemayoran Hospital from January 2023 to June 2023.
2. Babies experiencing jaundice at Gatot Subroto Army Hospital, Hermina Hospital Depok, and Hermina Hospital Kemayoran from January 2023 - June 2023.

Exclusion Criteria

The exclusion criteria in this study are:

1. Babies who experience neonatal jaundice which occurs during the first 24 hours after birth.
2. Babies diagnosed with other diseases by the doctor responsible for the baby.
3. Babies who do not have jaundice

Data Retrieval and Collection Procedures

The procedure for collecting and collecting data in this research began by requesting a certificate from FK UKI to conduct research. Then make a permission letter to the head of the IKA department of RSPAD Gatot Subroto, Hermina Hospital Depok, and Hermina Hospital Kemayoran to ask for a

permission letter to conduct research at these hospitals. Next, make a permission letter to the medical records installation for data collection.

Research Stages

1. How to Collect Data

Data collection was carried out at Gatot Sulbroto Army Hospital, Hermina Depok Hospital, and Hermina Kemayoran Hospital using medical records. Initially, the data obtained will be filtered again according to the Inclusion Criteria and Exclusion Criteria that have been determined, so that data is produced that will be used in the results of this research.

Data Processing Method

The data that has been collected was processed by using the IBM SPSS (Statistical for Social Science) program for Windows Edition 26.0 and the Microsoft Office Elxcell 2021 program with the following stages:

a. Editing Data
   In this activity, the researcher will check the completeness of the response answers on each lecture sheet that has been collected. However, if the researcher produces data that is less than complete, then the researcher will ask for the final response to complete it at the data collection location.
b. Data Coding
   This activity involves submitting a final number of numerical codes (numbers) for each course answer that has been submitted. This was done to facilitate data analysis.
c. Entry Data
   In this activity is after collecting data from the field, the research team compiles the data and answer codes that have been completed in the class questionnaire in the SPSS (Statistical Product and Selvicel Solution) program.
d. Data Cleaning
   In this process, researchers will carry out checks on the data that has been entered, to see whether there are errors.
e. Tabulation
   The data that has been entered was analyzed and presented in the form of a data table.

RESULT

Research result

This research is about Factors Associated with Neonatal Jaundice at Gatot Subroto Army Hospital, Hermina Depok Hospital, and Hermina Kemayoran Hospital. The data taken is primary data obtained through qualitative methods using medical record data. The samples were babies who met the inclusion criteria, namely with neonatal jaundice at the Gatot Subroto Army Hospital and 300 research samples were obtained. From the research results, data was obtained that had been processed in table form consisting of research variables. Characteristics of respondents based on gender, type of childbirth, birth weight, consumption of breast milk/formula milk, and gestational age, are presented in Table 1 below:

Table 1. Characteristic of Respondent

Variable	Number of Patients	
	Number (N)	Percentage (%)
Gender		
• **Male**	114	38
• **Female**	186	62
Type of Childbirth		
• **Sectio**	244	81
• **Spontaneous**	56	19
Birth Weight		
• **<2500 gram**	66	22
• **≥2500 gram**	234	78
Consumption of breast milk/formula milk		
• **Breast Milk**	165	55

• **Formula Milk**	135	45
Gestational Age		
• **<37 Week**	56	19
• ≥37 week	244	81

Based on table 1, it shows that the majority of research respondents were 186 male respondents with a percentage of 62% and 114 research respondents were female with a percentage of 38%. Based on the type of delivery, 244 respondents performed Sectio with a percentage of 81% and 56 research respondents spontaneously with a percentage of 19% with birth weight in the study being ≥2500 grams with a percentage of 234 respondents with a percentage of 78% and <2500 grams with a percentage of 66 research respondents with a percentage of 22%. The results of the respondent data show that the majority since birth have consumed breast milk by 165 respondents with a percentage of 55% and 135 respondents have consumed Formula Milk with a percentage of 45%. Based on the majority, the gestational age of mothers was ≥37 weeks, there were 244 respondents with a percentage of 81% and <37 weeks, there were 56 research respondents with a percentage of 19%.

Data on jaundice babies for each hospital that is the research locus, namely: Gatot Subroto Army Hospital, Kemayoran Hospital, and Hermina Depok Hospital, are presented in tables

Table 2. Data On Jaundice Babies at Gatot Subroto Army Hospital, Kemayoran Hospital, and Hermina Depok Hospital

Hospital	Number of Neonatal Jaundice Babies	Percentage (%)
Gatot Subroto Army Hospital	86	28.7
Kemayoran Hospital	79	26.3
Hermina Depok Hospital	135	45
Total	**300**	**100**

The relationship between gender and neonatal jaundice was obtained by analysis using chi-square with a p-value of 0.000 as presented in Table 3 below.

Table 3. Relationship between Gender and Neonatal Jaundice

Gender	Neonatal Jaundice		*p-value*
	Yes	**No**	
Female	114	0	0.000
Male	186	0	
Total	**300**	**0**	

Based on Table 3, it can be seen that gender has a p-value (0.000) < 0.05, which means it has a relationship with the incidence of neonatal jaundice**.**

Furthermore, data regarding the relationship between type of childbirth and neonatal jaundice is presented in table 4 below:

Table 4. Relationship between Type of Childbirth and Neonatal Jaundice

Types of Childbirth	Neonatal Jaundice		*P-Value*
	Yes	**No**	0.188
Sectio	244	0	
Spontaneous	56	0	
Total	300		

Based on Table 4, it can be seen that the type of delivery has a p-value> 0.05, which means it has no relationship with the incidence of neonatal jaundice.

The relationship between Birth Weight and Neonatal Jaundice is presented in Table 5 below:

Table 5. Relationship between Birth Weight and Neonatal Jaundice

Birth Weight	Neonatal Jaundice		*P-Value*
	Yes	No	
<2500 gram	66	0	0.118
>2500 gram	234	0	
Total	**300**	**0**	

Based on Table 5, it can be seen that the baby's birth weight has a p-value> 0.05, which means it has no relationship with the occurrence of neonatal jaundice.

The relationship between consumption of breast milk/formula milk and neonatal jaundice is presented in Table 6 below:

Table 6. Relationship between Consumption of Breast Milk/Formula Milk and Neonatal Jaundice

Consumption of Breast Milk/Formula Milk	Neonatal Jaundice		*P-Value*
	Yes	No	
Breast Milk	165	0	0.001
Formula Milk	135	0	
Total	**300**	**0**	

Based on Table 6, it can be seen that the consumption of breast milk/formula milk has a p-value (0.001) < 0.05, which means it has a major association with the incidence of neonatal jaundice.

The relationship between Gestational Age and Neonatal Jaundice is presented in Table 7 below:

Table 7. Relationship between Gestational Age and Neonatal Jaundice

Gestational Age	Neonatal Jaundice		*P-Value*
	Yes	No	
<37 Week	56	0	0.001
>37 Week	244	0	
Total	**300**	**0**	

Based on Table 7, it can be seen that the mother's gestational age has a p-value> 0.49, which means it has no relationship with the incidence of neonatal jaundice.

DISCUSSION

The Relationship between Gender and Neonatal Jaundice

In this study, it was discovered that there was a significant relationship between gender and the incidence of neonatal jaundice (p=0.000). In this study, 114 female babies experienced neonatal jaundice and 186 male babies experienced neonatal jaundice. The results of this research are in line with research by Intan Parulian, et al in 2017 which showed that there was a significant relationship between gender and neonatal jaundice (p=0.000) with a total of 56 male babies and 39 female babies. In male babies, bilirubin is produced more quickly than in girls, this is because male babies have protein Y in the liver which plays a role in transporting bilirubin to liver cells. In baby girls, there are two x_1 chromosomes that balance red blood cell enzymes [15].

Neonatal jaundice is mostly in male neonates because men have a higher risk of jaundice compared to women due to several influencing factors, such as (1) The prevalence of Gilbert's Syndrome (a genetic disorder of bilirubin conjugation) is twice as high as in men. (12.4%) compared to women (4.8%); (2) Glucose-6-phosphate dehydrogenase (G6PD) deficiency, which is an enzyme disorder linked to the sex chromosome (X-linked) which generally only manifests in males. 16 G6PD deficiency results in a severe defect in the activity of the gene encoding the enzyme in both a thread in the chromosome chain or a defect in the partner's allele that is inherited from the

mother so that it cannot replace the function of the partner's damaged allele. If the amount of the G6PD enzyme is insufficient, red blood cells will break more easily [17].

Relationship between type of delivery and neonatal jaundice

In this study, 244 babies born by cesarean section experienced jaundice, while 56 babies born spontaneously vaginally had jaundice. Research by Apsari, et al in 2023 is in line with this research, where as many as 136 babies born by cesarean section (72.3%) experienced jaundice and as many as 52 babies born spontaneously vaginally (27.7%) experienced jaundice [18]. Based research by Yazdiha, et al in 2018 showed that giving birth by cesarean section has a 2.88 times greater risk of experiencing neonatal jaundice compared to vaginal birth [19].

Sectio caesarea (SC) is an artificial incision in the abdominal wall and uterine wall to deliver the fetus provided the uterus is intact and the fetus weighs above 500 grams. Babies born with cesarean section tend not to receive the beneficial bacteria found in the mother's birth canal, these bacteria influence the maturation of the body's immune system, so babies born with cesarean section are more easily infected. Mothers who give birth by cesarean section rarely breastfeed their babies directly because of post-operative discomfort, where breast milk plays a role in inhibiting the enterohepatic circulation of bilirubin in neonates [18].

Relationship between Birth Weight and Neonatal Jaundice

Based on the results of the birth weight of research respondents, it shows that the majority of birth weights in the study were >2500 grams, 234 respondents experienced neonatal jaundice with a percentage of 78% and <2500 grams, 66 respondents experienced neonatal jaundice in the study with a percentage of 22%. This is in line with research conducted by Ramdani & Sutrisna M in 2022, namely that of 20 LBW respondents, there were 75.0% or 15 respondents were jaundiced, and 25.0% or 5 respondents were not jaundiced. Of the 35 respondents who were not LBW, there were 17.1% or 6 respondents were jaundiced, and 82.9% or 35 respondents were not jaundiced [20]. The results of the study were in line with research by Latifah, et al. It was found that the risk of LBW was 8,820 times greater than in neonates with birth weight babies. Normal [21].

Jaundice experienced by babies with Low Birth Weight (LBW) is caused by the immaturity of the baby's liver function to process erythrocytes. In babies, the lifespan of red blood cells is approximately 90 days and then the erythrocytes must be processed by the baby's liver as a result of their breakdown. At birth, the baby's heart is not good enough to do its job. The remainder of the breakdown of erythrocytes is called bilirubin, this bilirubin is what causes jaundice in babies and if the amount of bilirubin accumulates in the body, the bilirubin can stain the skin and other body tissues [21].

In babies with LBW, it can cause the absence or reduction in the number of enzymes or cause a reduction in bilirubin reduction by liver cells. Apart from that, babies with LBW experience an increase in serum bilirubin slightly slower than the increase in bilirubin in full-term babies, a longer period can result in bilirubin levels 22 In addition, LBW babies can increase the risk of infection due to decreased maternal immunoglobulin reserves, damage to the ability to form antibodies and the integumentary system, as well as incomplete liver maturity causing the conjugation of unconjugated bilirubin to incomplete conjugated bilirubin [21].

The results of bivariate and multivariate analysis research show that there is a relationship between LBW and consumption of breast milk/SUFOR on the incidence of neonatal jaundice. This is in line with research by Nimas Anggie Auliasari, et al (2019) using the Contingency coefficient test with a level of significance (α=0.05) indicating there is a relationship between LBW and the incidence of neonatal jaundice at Dr. Soetomo. The OR value obtained was

0.346. This means that LBW babies are 3 times more likely to get jaundice than babies who are not LBW [23].

The relationship between consumption of breast milk or formula milk and neonatal jaundice

In this study, it was discovered that the majority of respondents from birth consumed breast milk, with 165 respondents with a percentage of 55% experiencing neonatal jaundice and 135 respondents consuming formula milk (SUFOR) with a percentage of 45% experiencing neonatal jaundice. This is in line with research conducted by Rahmadani in 2022, namely. In this research, it was discovered that of the 26 respondents who gave breast milk <12 times a day, there were 76.9% or 20 respondents who were jaundiced and 23.1% or 6 respondents who were not jaundiced. Of the 29 respondents who breastfed ≥12 times a day, there were 2.4% or 1 respondent had jaundice, and 96.6% or 28 respondents did not have jaundice [20].

Babies who received breast milk, when compared with babies who received formula milk, had higher levels of bilirubin which was related to the release of intake in the first few days of life. In babies whose supply of breast milk supplements is low or does not produce abundance, this will result in reduced stimulation of the digestive system (intestines) because, during the 0 - 28 day old age, the baby only consumes breast milk. A lack of caloric intake can increase the circulation of enterohepatic and adequate methylation mechanisms in cells thereby reducing the intensity of the increase in bilirubin at the beginning of life due to the initial release of meconium from the digestive tract of the cell thereby preventing the recirculation of bilirubin from the digestive tract through the portal-systemic circulation. Babies who experience a shortage of breast milk cause the levels of bilirubin that should normally be circulated with feces to accumulate in the blood cells until jaundice occurs. To control bilirubin levels in newborn babies, it is recommended to purchase breast milk as early as possible. Babies who are given early drinking and colostrum supplementation can reduce the incidence of physiological hyperbilirubinemia. Effective breast milk delivery includes the correct frequency, duration, and procedures for giving breast milk [20].

Based on the American Academy of Pediatrics in 2004 regarding the prevention and treatment of hyperbilirubinemia in newborns. Prevention by providing breast milk as soon as possible is an important effort, as frequent breastfeeding reduces enterohepatic shunt, supports the stability of normal bacterial flora, and stimulates small intestinal activity.

It is recommended to give breast milk to babies every 2-3 hours or 8-12 times a day in the first few days because decreased calorie intake can cause dehydration and can cause jaundice. Jaundice is divided into three types: physiological jaundice, pathological jaundice, and kernicterus. Physiological jaundice is jaundice that appears in babies aged the second and third days which has no pathological basis, the levels do not exceed dangerous levels. Pathological jaundice is jaundice that has a pathological basis or excessive bilirubin levels, which is called hyperbilirubinemia. Physiological jaundice caused by other factors such as inadequate drinking for the baby or inadequate calorie or fluid intake will reduce the incidence of early jaundice due to breast milk. Babies who are given water early or more often and babies who pass meconium earlier are less likely to experience physiological jaundice. Babies who are breastfed have lower bilirubin levels and tend to defecate more frequently [20].

The Relationship between Gestational Age and Neonatal Jaundice

The relationship between maternal gestational age and neonatal jaundice in this study showed that there was no significant relationship (p=0.494) with gestational age < 37 weeks for 56 respondents and > 37 weeks for 244 respondents. The results of this research are in line with research conducted

by Suci S, et al at the Mulhammadiyah Hospital in Palembang which showed that 66 respondents (82.5%) had jaundice at term gestation, which was greater than 9 respondents (11.3%) at preterm gestation. and post-term gestational age of 5 respondents (6.3%) and p-value = 0.069.

Generally, neonatal jaundice is more often experienced by premature babies due to excessive destruction of red blood cells, immature liver, and gastrointestinal tract. Postnatal liver maturation in premature babies makes the process of bilirubin uptake and conjugation slower. Bilirubin levels increase early, then reach a peak (5-7 days) and remain elevated for longer. In addition, delay in providing enteral feeding in the clinical management of sick premature newborns can limit intestinal motility and bacterial colonization resulting in a further increase in enterohepatic circulation of bilirubin.

CONCLUSION

Based on the results of the research I conducted entitled Factors associated with neonatal jaundice at Gatot Subroto Army Hospital, Hermina Depok Hospital, and Hermina Kemayoran Hospital, it can be concluded that:

1. From the research, it was found that 300 subjects were patients with neonatal jaundice who met the criteria. As many as 62.3% of research subjects were female (n=187), and 37.7% were male (n=113). Of the total subjects, 76.3% (n=229) of patients were born at term above 37 weeks and 23.7% of patients were born under 37 weeks (n=71). The most common types of delivery were cesarean section at 81.3% (n=244) and spontaneous at 18.7% (n=56).
2. From the results obtained, the factors that influence neonatal jaundice are the gender of the baby (p=0.000) and consumption of breast milk or formula (p=0.001).
3. Maternal nutrition during pregnancy affects jaundice in newborn babies.

Declaration by Authors

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