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# The characteristic of neonatal hyperbilirubinemia before and after phototherapy at Sanglah Hospital, Denpasar, Bali in 2017

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## ABSTRACT

**Background:** Hyperbilirubinemia is the most clinical problem in newborn babies. Hyperbilirubinemia occurs 60% in aterm babies and 80% in premature babies. This study aims to know the incidence of hyperbilirubinemia, characteristics of hyperbilirubinemia and effect of phototherapies to bilirubin levels.

**Methods:** A cross-sectional retrospective study was conducted using medical records among 94 neonates with hyperbilirubinemia who treated with phototherapies at Sanglah hospital during 2017. Data regarding gender, gestational weeks, type of delivery, size for gestational age, the onset of hyperbilirubinemia, etiology, birth weight, maternal gravid status, and bilirubin levels were collected and analyzed using SPSS version 20 software descriptively.

**Results:** From 94 neonatal hyperbilirubinemia that meet the inclusion criteria, 51 (54.3%) males and 43 (45.7%) females based on gender. Mean gestational ages were 36.35±2.921 weeks. The major etiology of neonatal hyperbilirubinemia were breastfeeding jaundice 33 (25.8%), Prematurity 23 (18.7%), ABO incompatibility 13 (10.6%), Breast milk jaundice 11 (8.9%), gastrointestinal malformation 6 (4.9%), G6PD deficiency 5 (4.1%), and sepsis 3 (2.4%). The mean total bilirubin prior to phototherapy was 15.6 ± 4.11 mg/dL whereas the indirect bilirubin was 14.56 ± 3.55 mg/dL. The duration of phototherapy in this study was 2.8±0.65 days.

**Conclusions:** The incidence of neonatal hyperbilirubinemia during 2017 at Sanglah Hospital were predominantly caused by breastfeeding jaundice, prematurity, and ABO incompatibility. There were decreased bilirubin levels following phototherapies.

**Keywords:** Hyperbilirubinemia, Neonates, Phototherapy

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## INTRODUCTION

Hyperbilirubinemia is a clinical condition in infants characterized by staining of jaundice on the skin and sclera due to elevated serum bilirubin levels. Hyperbilirubinemia is one of the most common clinical phenomena in neonates occurring in the first week of life. Most of the incidence of neonatal jaundice is physiological, but non-physiologic ones should be aware because it can cause severe complications of both residual and fatal symptoms due to late treatment.[1,2,3]

Hyperbilirubinemia is present in approximately 60% of term infants and 80% of premature infants. The incidence rate shows that over 50% of newborns have clinically detectable jaundice within the first week of life. In the United States, of the 4 million neonates born every year, about 65% of them experience jaundice. In Malaysia, the study conducted in 1998 at government hospitals and health centers under the Ministry of Health found that 75% of newborns had jaundice within the first week of life. In Indonesia, hyperbilirubinemia cases were obtained from several educational hospitals. A cross-sectional study conducted at the National Cipto Mangunkusumo in 2003 found the prevalence of hyperbilirubinemia in newborns with bilirubin levels above 5 mg/dL was 58% and 29.3% with bilirubin levels above 12 mg / dL at week first life.[3,4]

Hyperbilirubinemia can be distinguished in two types, namely physiological and pathological. Physiologic neonatal jaundice arises from the increase and accumulation of indirect bilirubin <5 mg/dl / 24 hours. This is because neonatal bilirubin metabolism is still in transition from fetal to adulthood. Pathologic hyperbilirubinemia is also jaundice arising within the first 24 hours in which the increase and accumulation of indirect bilirubin > 5 mg/dl / 24 hours. Hyperbilirubinemia will persist for up to 8 days or more in term infants, whereas in premature infants jaundice will remain there until day 14 or more. Pathologic hyperbilirubinemia may be caused by several diseases such as hemolytic anemia, polycythemia, extravasation of blood (hematoma), excessive enterohepatic circulation, conjugate defects, reduced bilirubin uptake by hepatic, disruption of direct bilirubin transport

out of the hepatocytes or by obstruction of bile flow. Risk factors considered to be the triggers of hyperbilirubinemia include premature pregnancy, low birth weight infants, pathological labor, asphyxia, premature rupture of membranes, turbid membranes and maternal and infant blood group incompatibility.[4,5]

Hyperbilirubinemia can cause bilirubin encephalopathy, known as kernicterus, if not treated well. Kernicterus results from the accumulation of indirect bilirubin in the central nervous system that exceeds the limit of bilirubin toxicity in the basal ganglia and hippocampus.[4,5] Neonatal jaundice should get attention and good handling to reduce infant mortality rate (IMR) which still high in Indonesia. The IMR of neonatal jaundice in Indonesia in 1997 was found 41.4 per 1000 live births. Kernicterus can also cause residual symptoms of cerebral palsy, hearing loss, paralysis and dental dysplasia that greatly affect the quality of life.[4,5]

Based on the issue above, a preliminary study regarding hyperbilirubinemia among neonates need to be carried out in order to prevent those mention above. So that, this study aims to know the characteristic neonatal hyperbilirubinemia before and after phototherapy at Sanglah Hospital, Denpasar, Bali in 2017.

## MATERIALS AND METHODS

### Subject Criteria

A cross-sectional study among 94 neonates, has been conducted in Neonatology ward at Sanglah Hospital, Bali during January-December 2017 period. The subjects were all neonatal patients with hyperbilirubinemia who treated in Neonatology ward and meet the inclusion criteria. The inclusion criteria in this study were hyperbilirubinemia patients with aged 0-30 days who underwent treatment during study period. Incomplete medical records were the exclusion criteria in this study.

### Data Analysis

The characteristics used in this study included gender, gestational age, mother parity, birth weight, infant diagnose, plasma bilirubin values before phototherapy, duration of phototherapy, and plasma bilirubin levels before and after phototherapy. Data obtained from the patient's medical record at Medical Record Installation during the study period. This study has been approved by the Research Ethics Committee of the Faculty of Medicine, Udayana University/Sanglah General Hospital. The study was conducted under the supervision of Neonatology Division, Medical Faculty of Udayana University. Data were presented in a descriptive form related mean, standard deviation, and the percentage using SPSS version 20 software.

## RESULTS

Based on the medical records, there were 137 (12.7%) infants with hyperbilirubinemia. However, we only found 94 neonates who meet the inclusion criteria. From them, there were 51 (54.3%) males and 43 (45.7%) females. Mean gestational ages were 36.35±2.921 weeks. The onset of hyperbilirubinemia was 3.67 days for term babies and 2.25 days for preterm babies. Etiology in this study were breastfeeding jaundice 33 babies (25.8%), Prematurity 23 babies (18.7%), ABO incompatibility 13 babies (10.6%), Breast milk jaundice 11 babies (8.9%), Gastrointestinal malformation 6 babies (4.9%), G6PD deficiency 5 babies (4.1%), and sepsis 3 babies (2.4%). Demographic characteristics of neonates with hyperbilirubinemia are shown in Table 1.

Phototherapy was the most procedure in this study, there was no exchange transfusion therapy founds in this study. Prior to phototherapy, the mean total bilirubin was 15.59±4.11 mg/dL, followed by direct bilirubin was 0.89±0.73 mg/dL, and indirect bilirubin was 14.56±3.55 mg/dL. The maximum total bilirubin levels before phototherapy were 30.03 mg/dL meanwhile minimum values 10.32 mg/dL. The maximum amounts of indirect bilirubin were 26.76 mg/dL meanwhile minimum values 10.24 mg/dL.. The duration of phototherapy in this study was 2.8±0.65 days. The mean total bilirubin after phototherapy was 9.21 ± 2.64 mg/dL, direct bilirubin 1.23±1.49 mg/dL, and indirect bilirubin levels were 8.11±2.62 mg/dL. The characteristic of bilirubin values shown in Table 2.

## DISCUSSION

Hyperbilirubinemia is the major problem in neonates. The incidence of hyperbilirubinemia in the United States is 65%. Nigeria, a study conducted by Chime in 2011 found the frequency of hyperbilirubinemia around 33% (21% males and 12% females). The frequency of hyperbilirubinemia in Indonesia itself on mature baby based on varies from 13.7% to 85%.[1,2,3,4]

Our study found that the majority of infants with hyperbilirubinemia dominantly were males compared with females. In our study hyperbilirubinemia also predominantly occurred in aterm infants compare with the premature. This result may cause the incidence of hyperbilirubinemia in premature infants is lower than aterm infants. However, there are differences results found with

**Table 1** The characteristics of neonatal hyperbilirubinemia based on demographics

| Characteristics | n (%) | Mean±SD |
|---|---|---|
| **Gender** | | |
| - Male | 51 (54.3%) | |
| - Female | 43 (45.7%) | |
| **Gestational Weeks (mean)** | | 36.35±2.921 |
| - Preterm | 31 (33%) | |
| - Aterm | 63 (67%) | |
| - Postterm | - | |
| **Type of delivery** | | |
| - Sponateus | 48 (51.1%) | |
| - Caesarian | 23 (24.5%) | |
| - Vacuum extraction | 15 (16%) | |
| - Forceps delivery | 8 (8.5%) | |
| **Size for gestational age** | | |
| - Appropriate for gestational age | 82 (87.2%) | |
| - Small for gestational age | 8 (8.5%) | |
| - Large for gestational age | 4 (4.3%) | |
| **Onset of hyperbilirubinemia (days)** | | |
| - Preterm babies | 2.25 | |
| - Aterm babies | 3.27 | |
| **Etiology** | | |
| - Breast feeding jaundice | 33 (25.8%) | |
| - Prematurity | 23 (18.7%) | |
| - ABO incompability | 13 (10.6%) | |
| - Breast milk jaundice | 11 (8.9%) | |
| - Gastrointestinal malformation | 6 (4.9%) | |
| - G6PD deficiency | 5 (4.1%) | |
| - Sepsis | 3 (2.4%) | |
| **Birth Weight (gram)** | | |
| - <1000 | 3 (3.2%) | |
| - < 1500 | 8 (8.5%) | |
| - 1500- 2500 | 21 (22.3%) | |
| - >2500 | 62 (66%) | |
| **Maternal gravid status** | | |
| - Primivara | 19 (20.2%) | |
| - Multivara | 75 (79.8%) | |

**Table 2** Bilirubin levels before and after phototherapy

| Variables | Mean ± SD | Minimum-maximum (mg/dL) |
|---|---|---|
| Bilirubin values before phototherapy (mg/dL) | | |
| Total bilirubin | 15.59 ± 4.11 | |
| Direct bilirubin | 0.89 ± 0.73 | 10.32-30.03 |
| Indirect bilirubin | 14.56 ± 3.55 | |
| Bilirubin values after phototherapy (mg/dL) | | 10.24-26.76 |
| Total bilirubin | 9.21 ± 2.64 | |
| Direct bilirubin | 1.23 ± 1.49 | |
| Indirect bilirubin | 8.11 ± 2.62 | |
| Duration of phototherapy (days) | 2.8 ± 0.65 | |

the previous studies.[6,7] The previous studies found that hyperbilirubinemia occurred more frequently and a longer time in late-preterm infants (Infants birth at 34 0/7 weeks to 36 6/7 weeks of gestation) than aterm.[6,7] This may be caused by the maturation-delayed of late-preterm infants and low concentrations of uridine glucuronosyltransferase diphosphoglucuronate.[8,9,10,11]

Our study found that hyperbilirubinemia primarily related to breastfeeding jaundice. Breastfeeding jaundice occurs within the first week of life and overlaps with the breast milk jaundice and physiologic jaundice.[11] This condition is the result of inadequate breast milk volume and neonatal volume contraction relative to the amount of bilirubin. Inadequate oral intake can reduce bowel movement or bilirubin excretion which lead to hyperbilirubinemia conditions.[12,13,14]

The amounts of premature babies who got hyperbilirubinemia in this study were quite high. Based on the clinical diagnosis, the prematurity condition was taken on the second place as a cause of hyperbilirubinemia. Some of the premature babies overlap with sepsis condition that can cause the hyperbilirubinemia. Hyperbilirubinemia in preterm infants was more prevalent, severe, and protracted than in term neonates, as a result of the exaggerated neonatal red cell, hepatic, and gastrointestinal immaturity. A delay in the initiation of enteral feedings so common in the clinical management of sick premature newborns may limit intestinal flow and bacterial colonization resulting in further enhancement of bilirubin enterohepatic circulation.[15,16,17]

Many newborns, especially small infants (birth weight <2500 grams or gestational age <37 weeks) had jaundice in the first few weeks his life. Hyperbilirubinemia in infants newborns is present in 25-50% aterm neonates and even higher on preterm neonates. Jaundice in infants newborn is a physiological phenomenon or may be pathological. Infection that can cause the occurrence is an infection that occurs in periods or periods organogenesis, i.e. in the trimester first pregnancy.[10,13,14]

The third etiology caused hyperbilirubinemia in our study was The ABO incompatibility. The ABO incompatibility becomes the most common cause of iso-immune hemolytic disease of the newborn in developed countries. The previous study of newborns in Turkey found that there were 14.8% ABO incompatibility cases whereas 21.3% of them is exhibiting a significant hyperbilirubinemia and 4.4% for severe ABO hemolytic disease.[7,9] In general, hemolysis due to ABO incompatibility is minimal, and the clinical course is relatively benign due to the relatively fewer group A or B antigenic sites on neonatal red blood cells. However, severe cases

demonstrating aggressive hemolysis and hydrops fetalis condition have also been reported.[7,9,12]

Hyperbilirubinemia can be occurred caused by the contact with substances that stimulate red blood cells to destruction which lead to jaundice. Genetic abnormalities are also responsible for different cases of hyperbilirubinemia, such as G6PD, whereas this enzyme-deficiency is usually more susceptible among males due to only have one single X-chromosomes comparing with females. According to study conducted by Iesje in 2007, the lack of a G6PD enzyme in the red blood cell wall leads to premature destruction of RBC and resulting in bilirubin increased.[4,6,7]

Besides of G6PD, the intestinal problem in neonates also contributes to the increased risk of hyperbilirubinemia. Obstructive jaundice is a particular type of jaundice and occurs when the essential flow of bile to the intestine is blocked and remains in the bloodstream. This might be due to blocked bile ducts caused biliary atresia, duodenal atresia, and pancreas annular which can block the area where the bile duct meets the duodenum. Some study that conducted by Aoshima Naoya finds that inadequate calorie intake or starvation has been suggested as a cause of neonatal jaundice, which can further cause permanent brain damage, kernicterus. In his study experimentally investigated whether additional glucose treatments induce the bilirubin-metabolizing enzyme – UDP-glucuronosyltransferase (UGT) 1A1 – to prevent the onset of neonatal hyperbilirubinemia.[2,18]

Phototherapy is the main therapy that is often used in the cases of hyperbilirubinemia. This therapy is more commonly used because of milder side effect compared with exchange transfusion. Phototherapy converts indirect bilirubin to isomerization of water-soluble bilirubin.[16-18] A study conducted by Maharoof showed a decreased in the average of bilirubin up to 3.26 mg/dL in 24 hours.[18] The study also found no significant efficacy difference in reducing indirect bilirubin. Our study found that phototherapy also effective in decreasing total bilirubin and indirect bilirubin similar to the previous study mentioned above.

## CONCLUSION

The incidence of neonatal hyperbilirubinemia in Sanglah Hospital during 2017 was about 13.2 %. The most common causes of neonatal hyperbilirubinemia in neonatology ward were breastfeeding jaundice, prematurity, and ABO incompatibility. There was a decreasing level of total bilirubin, direct, and indirect bilirubin following phototherapy.

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