

Associated Factors and Causes of Neonatal Jaundice in Term Neonates Needing Phototherapy

Fatores Associados e Causas de Icterícia Neonatal em Bebês a Termo com Necessidade de Fototerapia

Factores Asociados y Causas de Icterícia Neonatal en Recién Nacidos a Término que Requieren Fototerapia

RESUMO

Objetivo: Avaliar os fatores associados e as causas da icterícia neonatal em bebês a termo com necessidade de fototerapia. **Método:** Estudo observacional, transversal e prospectivo incluiu 187 recém-nascidos a termo que desenvolveram icterícia neonatal com necessidade de fototerapia. As variáveis foram apresentadas como porcentagens, médias ou medianas. Valor de $p < 0.05$ foi considerado estatisticamente significativo. **Resultados:** Os fatores associados mais comuns foram clameamento tardio do cordão umbilical (59.9%) e idade materna > 25 anos (57.2%). As causas mais frequentes foram incompatibilidade ABO (40.1%) e icterícia do aleitamento materno (31.6%). Na icterícia não hemolítica, a idade materna > 25 anos foi o fator associado significativo ($p < 0.001$). **Conclusão:** A identificação precoce dos fatores associados e das causas de hiperbilirrubinemia é importante para o manejo efetivo desses bebês, visando diminuir o tempo de internação e chance de sequelas.

DESCRIPTORES: Icterícia; Hiperbilirrubinemia; Recém-nascido.

ABSTRACT

Objective: To Evaluate associated factors and causes of neonatal jaundice requiring phototherapy in term neonates. **Method:** Observational and prospective cross-sectional study included 187 term infants that developed neonatal jaundice and required phototherapy. Variables were presented as percentages, mean or median. P value < 0.05 was considered statistically significant. **Results:** The most common associated factors found were delayed umbilical cord clamping (59.9%) and maternal age > 25 years (57.2%). The most frequent causes were ABO incompatibility (40.1%) and breastfeeding jaundice (31.6%). In nonhemolytic disease, maternal age > 25 years was found as a associated factor ($p < 0.001$). **Conclusion:** Early identification of associated factors and causes of jaundice is important for the effective management of these newborns, aiming to reduce the length of stay and chance of sequelae.

DESCRIPTORS: Jaundice; Hyperbilirubinemia; Newborn.

RESUMEN

Objetivo: Evaluar los factores asociados y las causas de la ictericia neonatal en recién nacidos a término que requieren fototerapia. **Método:** Estudio observacional, transversal y prospectivo incluyó 187 recién nacidos a término que desarrollaron ictericia neonatal que requirió fototerapia. Las variables se presentaron como porcentajes, medios o medianos. El valor $P < 0.05$ se considero estadísticamente significativo. **Resultados:** Los factores asociados más comunes fueron el retraso en el pinzamiento del cordón umbilical (59.9%) y la edad materna > 25 años (57.2%). Las causas más frecuentes fueron la incompatibilidad ABO (40,1%) y la ictericia derivada de la lactancia materna (31,6%). En la ictericia no hemolítica, la edad materna > 25 años fue un factor asociado significativo ($p < 0.001$). **Conclusión:** La identificación precoz de los factores asociados y las causas de la hiperbilirrubinemia es importante para el manejo eficaz de estos lactantes, con el objetivo de reducir la estancia hospitalaria y la posibilidad de secuelas.

DESCRIPTORES: Ictericia; Hiperbilirrubinemia; Recién nacido.

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Daniela Hespanha Marinho
Pediatrician and Neonatologist – Professor with a PhD – Department of Pediatrics, UFPR – Clinical Hospital Complex, Federal University of Paraná, Curitiba, PR, Brazil.
ORCID: <https://orcid.org/0000-0002-9699-7241>

Bruna Mai dos Santos
Pediatric Residency Program – Clinical Hospital Complex, Federal University of Paraná, Curitiba, PR, Brazil.
ORCID: <https://orcid.org/0009-0006-9921-2813>

Maria Luiza Souza Nieto
Pediatric Residency Program – Clinical Hospital Complex, Federal University of Paraná, Curitiba, PR, Brazil.
ORCID: <https://orcid.org/0000-0002-6210-9584>

Regina Paula Guimarães Vieira Cavalcante da Silva
Pediatrician and Neonatologist – Professor with a PhD – Department of Pediatrics, Clinical Hospital Complex, Federal University of Paraná, Curitiba, PR, Brazil.
ORCID: <https://orcid.org/0000-0002-2467-1760>

Paulyne Stadler Venzon
Pediatrician and Neonatologist – Professor with a PhD – Department of Pediatrics, Clinical Hospital Complex, Federal University of Paraná, Curitiba, PR, Brazil.
ORCID: <https://orcid.org/0000-0002-2976-5205>

Patricia Povaluk
Pediatrician and Neonatologist with a Master's Degree – Clinical Hospital Complex, Federal University of Paraná, Curitiba, PR, Brazil.
ORCID: <https://orcid.org/0000-0001-5086-5270>

Fabiano Steil da Silva
Pediatrician and Neonatologist – Professor with a Master's Degree – Department of Pediatrics, Clinical Hospital Complex, Federal University of Paraná, Curitiba, PR, Brazil.
ORCID: <https://orcid.org/0000-0003-1306-2182>

Carlos Alberto Fernandes Baltar
Pediatrician and Neonatologist – Professor with a Master's Degree – Department of Pediatrics, Clinical Hospital Complex, Federal University of Paraná, Curitiba, PR, Brazil.
ORCID: <https://orcid.org/0000-0002-7099-7008>

INTRODUCTION

Neonatal jaundice is the clinical manifestation of hyperbilirubinemia and is the most common cause of hospitalization in the first week of life among newborns.^{1,2,3} Hyperbilirubinemia occurs in approximately 60% of term infants and 80% of preterm infants.^{1,2,3, 4} It is defined as yellowing of the sclera, skin, and mucous membranes due to the accumulation of bilirubin.^{2,5,6,7} Approximately one in ten newborns develops clinically significant hyperbilirubinemia and requires monitoring and treatment.^{4,5,6}

Risk factors for neonatal hyperbilirubinemia include prematurity, maternal age, ABO and Rh incompatibility, drug use, maternal diabetes, maternal obesity, high altitude, polycythemia, cephalohematoma or hematomas, exclusive breastfeeding, excessive weight loss, sepsis, asphyx-

ia, genetic disorders, male sex, and certain ethnic groups (Asian ethnicity), delayed umbilical cord clamping, early jaundice before 24 hours of life, and a previous child (sibling of the newborn) with significant jaundice requiring phototherapy.^{5,6,7,9,10,11,12,13}

At a hospital belonging to the Baby-Friendly Hospital Initiative network, breastfeeding is a priority from the moment the baby is born due to its well-established benefits for the health of both the mother and the newborn.¹⁴

Phototherapy is the first-line treatment for indirect hyperbilirubinemia and is a safe procedure with rare adverse effects, although it prolongs the baby's hospital stay.^{5,6,12,13} Therefore,

it is important to identify newborns at higher risk of requiring treatment. This study aimed to evaluate the associated factors and causes of neonatal jaundice in term newborns who required phototherapy at a ter-

tiary hospital belonging to the Iniciativa Hospital Amigo da Criança network, given that public policies encourage the promotion of breastfeeding.

METHOD

This observational, analytical, cross-sectional, and prospective study was conducted in the Mother-Baby Room of a tertiary maternity ward at a hospital in southern Brazil belonging to the Baby-Friendly Hospital Initiative network and included full-term term newborns who developed neonatal jaundice requiring phototherapy between August 3, 2023, and August 2, 2024. Neonates with infections, genetic syndromes, those readmitted for phototherapy without a prior need for phototherapy, and those transferred to the Neonatal Intensive Care Unit (NICU) were excluded from the study.

The sample size was based on the expected prevalence of phototherapy need in term infants of approximately 6%, with a 95% confidence level and a 3% margin of error, resulting in a minimum sample size of 184 participants. Maternal information, including age during pregnancy, race, mode of delivery, previous illnesses, gestational conditions, substance use, and history of a previous child requiring phototherapy, were obtained from all mothers. Neonatal data, including sex, gestational age, birth weight, time of umbilical cord clamping, weight loss during hospitalization, feeding method, cause of jaundice, duration of phototherapy, and length of hospital stay, were also collected.

According to the unit's routine, every newborn was assessed daily by the medical care team for clinical jaundice and, additionally, at least once prior to discharge via transcutaneous bilirubin measurement. When the infant's transcutaneous bilirubin level was 2–3 mg/dL below the threshold for phototherapy, laboratory tests were ordered.¹⁵

The indication for phototherapy was based on the curve for newborns at 35 weeks' gestational age or older proposed by the American Academy of Pediatrics in 2004¹⁵ as this was the curve adopted by the department's physicians to indicate phototherapy.

Physiological jaundice was defined as a mild increase in indirect (unconjugated) bilirubin due to hepatic immaturity in the absence of any other disease or cause and without the need for phototherapy.^{8,13} Breastfeeding jaundice was defined as severe caloric deprivation evidenced by excessive weight loss due to insufficient lactation and/or inadequate transfer of breast milk to the newborn.¹⁴ ABO incompatibility jaundice was diagnosed when the mother had blood type O and her baby had type A or B, and in the presence of a positive direct Coombs test, an in-

creased reticulocyte count, or anemia (hematocrit below 40%).⁷ Rh incompatibility was diagnosed when the mother was Rh-negative and the baby was Rh-positive with a positive direct Coombs test.⁷ Idiopathic jaundice was defined as jaundice with no identified cause.⁹ Excessive weight loss was defined as weight loss greater than 7% within the first 48 hours of life or more than 10% after 48 hours of life.^{6,16} Polycythemia was diagnosed when the hematocrit level was greater than or equal to 65%.^{7,9} Delayed umbilical cord clamping was defined as clamping more than 60 seconds after birth.¹² ABO group incompatibility, Rh incompatibility, and glucose-6-phosphate dehydrogenase (G6PD) were classified as hemolytic diseases, and other diseases or causes of jaundice (except idiopathic jaundice) were classified as non-hemolytic diseases.⁶

Since the study did not include a control group of infants with jaundice who did not require phototherapy, some bivariate analyses were interpreted with caution to avoid potential confounding factors, such as creating a false association between the analyzed factors and jaundice requiring phototherapy.

Continuous variables were expressed as means and standard deviation (SD) or medians and interquartile range (IQR), depending on whether the distribution was symmetric or asymmetric. Categorical variables were expressed as absolute and relative frequencies. The difference between symmetric continuous variables was assessed using Student's t-test, and for asymmetric continuous variables, the Mann-Whitney U test was applied. For categorical variables, Pearson's chi-square test with Yates' correction was applied when appropriate. A p-value < 0.05 was considered statistically significant, and a 95% significance level was used for all tests (StatSoft, Inc. *STATISTICA*

(*statistical software*), version 12. Tulsa, OK: StatSoft, Inc.; 2013).

The study was approved by the Ethics Committee for Research Involving Human Subjects at the Hospital de Clínicas Complex (CHC) of the Federal University of Paraná (UFPR) (CAAE 71306723.8.0000.0096/2023).

RESULTS

During the study period, 3,570 babies were born. Of this total, 3,117 were full-term newborns, and 2,951 babies were placed in rooming-in with their mothers. Of these 2,951 full-term newborns, 201 (6.8%) were diagnosed with indirect hyperbilirubinemia requiring phototherapy. Fourteen patients were excluded from the study (maternal refusal to participate: 9; congenital infection: 3; sepsis: 1; and need for transfer to the NICU: 1). The final sample consisted of 187 newborns.

The mean age of the mothers was 27.7 ± 6.7 years, and 110 (58.8%) were white. Most of the babies were born vaginally (77.0%). The median umbilical cord clamping time was 120 seconds (IQR 40–120). Ninety-two patients were male (49.2%). The mean gestational age was 38.6 ± 1.3 weeks, and the mean birth weight was 3134.4 ± 447.9 g. The median time to onset of jaundice was 25 hours of life (IQR = 18–36). The median time to initiation of phototherapy was 44 hours of life (IQR = 28–54). The median duration of phototherapy was 30 hours (IQR = 24–50). The mean length of hospital stay for these infants was 119.7 ± 35.9 hours (Table 1).

Table 1 – Maternal and neonatal demographic data (n= 187) in Curitiba, Paraná, Brazil (CHC – UFPR), 2023-2024

Maternal characteristics	Mean ± SD or n (%) or median (IQR)
Maternal age (years)	27.7 + 6.7
Race	
White	110 (58.8%)
Black	75 (40.1%)
Asian	2 (1.1%)
Parity	
Primiparous	94 (50.3%)
Multiparous	93 (49.7%)
Type of delivery	
Vaginal	144 (77.0%)
Cesarean section	43 (23.0%)
Umbilical cord clamping time (seconds)	120 (40-120)
Immediate	32 (17.1%)
Up to 60	43 (23.0%)
61 to 120	95 (50.8%)
≥ 121	17 (9.1%)
Previous child requiring phototherapy ^a	15(16.3%)
Neonatal Characteristics	
Male sex	92 (49.2%)
Gestational age (weeks)	38.6 + 1.3
Birth weight (g)	3134.4 + 447.9
Onset of jaundice (hours of life)	25.0 (18-36)
Total serum bilirubin at onset of jaundice (mg/dL)	10.6 + 2.8
Initiation of phototherapy (hours of life)	44.0 (28-54)
Total serum bilirubin at initiation of phototherapy (mg/dL)	12.4 + 3.2
Reticulocyte count (%)	5.4 (4.4-6.6)
Hematocrit (%)	52.1 + 7.1
Duration of phototherapy (hours)	30 (24-50)
Length of hospital stay (hours)	119.7 ± 35.9
Discharge weight (g)	2990.0 ± 438.1

SD: Standard deviation. n: number. IQR: Inter-quartile range. ^an: 92.
Source: The authors.

The maternal and neonatal factors associated with indirect hyperbiliru-

binemia are described in Table 2. Of the 187 newborns, 182 (97.3%) had at least one factor associated with neonatal jaundice. The most common associated factor was delayed umbil-

ical cord clamping (>60 s) (59.9%), followed by maternal age >25 years (52.7%) and male sex (49.2%). Weight loss was present in 59 new-

Table 2 – Associated factors and causes of hyperbilirubinemia (n=187) in Curitiba, Paraná, Brazil (CHC-UFPR), 2023–2024

Associated factors	Number (%)
Delayed umbilical cord clamping (>60 s)	112 (59.9%)
Maternal age >25 years	107 (57.2%)
Male sex	92 (49.2%)
ABO blood group incompatibility	84 (44.9%)
Gestational age (<38 weeks)	75 (40.1%)
Maternal obesity	61 (32.6%)
Weight loss	59 (31.6%)
Gestational diabetes mellitus/Diabetes mellitus	42 (22.5%)
Previous child requiring phototherapy ^a	15 (16.3%)
Low birth weight (<2500 g)	23 (12.3%)
Smoking and illicit substance use	20 (10.7%)
Rhesus factor incompatibility	15 (8.0%)
Cephalohematoma	5 (2.7%)
Polycythemia	4 (2.1%)
Maternal race (Asian)	1 (1.1%)
Causes	
ABO blood group incompatibility	75 (40.1%)
Breastfeeding jaundice	59 (31.6%)
Idiopathic jaundice	39 (20.9%)
Cephalohematoma	5 (2.7%)
Polycythemia	4 (2.1%)
Glucose-6-phosphate dehydrogenase deficiency	4 (2.1%)
Rhesus factor incompatibility	1 (0.5%)
Length of hospital stay (hours)	119.7 ± 35.9
Discharge weight (g)	2990.0 ± 438.1

Source: The authors.

The most common causes of jaundice are described in Table 2. ABO blood group incompatibility (40.1%) and breastfeeding jaundice (31.6%) were the most common causes of hyperbilirubinemia in these newborns. ABO blood group incompatibility

was the most common cause in infants with a gestational age of 38 weeks or more (41.0–54.5%), whereas in infants at 37 weeks it occurred in only 29.3%. Breastfeeding jaundice was the most frequent cause in newborns at 37 weeks (41.3%), while in other gestational ages it ranged from

21.2% to 22.8%. Idiopathic jaundice occurred at all gestational ages, ranging from 20.0% to 21.3%. A higher frequency of G6PD deficiency was observed only among newborns at 40 weeks ($p=0.04$) (Table 3).

Table 3 – Causes of jaundice by gestational age in Curitiba, Paraná, Brazil (CHC-UFPR), 2023–2024

Causes of jaundice	37 weeks (n = 75)	38 weeks (n = 33)	39 weeks (n = 39)	40 weeks (n = 40)	p
Rh incompatibility	1 (1,3%)	0 (0,0%)	0 (0,0%)	0 (0,0%)	1,00
ABO incompatibility	22 (29,3%)	18 (54,5%)	16 (41,0%)	19 (47,5%)	0,05
Breastfeeding jaundice	31 (41,3%)	7 (21,2%)	11 (28,1%)	10 (25,0%)	0,11
Idiopathic jaundice	16 (21,3%)	7 (21,2%)	8 (20,5%)	8 (20,5%)	0,99
Cephalohematoma	3 (4,0%)	1 (3,0%)	1 (2,6%)	0 (0,0%)	0,65
Polycythemia	2 (2,7%)	0 (0,0%)	2 (5,1%)	0 (0,0%)	0,33
G6PD deficiency	0 (0,0%)	0 (0,0%)	1 (2,6%)	3 (7,5%)	0,04

G6PD: Glucose-6-phosphate dehydrogenase. Pearson's chi-square test.

Source: The authors.

Original Article

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When comparing factors associated with the causes of jaundice (hemolytic, non-hemolytic, and idiopathic

jaundice groups), maternal age >25 years was observed more frequently in non-hemolytic jaundice ($p < 0.001$)

and a lower frequency of gestational age of 37 weeks in hemolytic jaundice ($p = 0.01$) (Table 4).

Table 4 – Associated factors compared across groups of causes of neonatal jaundice in Curitiba, Paraná, Brazil (CHC-UFPR), 2023–2024

Associated factors	Hemolytic Jaundice (n = 80)	Non-Hemolytic Jaundice (n = 68)	Idiopathic Jaundice (n = 39)	p
Delayed umbilical cord clamping (>60 s)	56 (70.0%)	52 (76.5%)	34 (87.2%)	0.11
Maternal age >25 years	38 (47.5%)	52 (76.5%)	17 (43.6%)	< 0.001
Gestational diabetes mellitus / Diabetes mellitus	16 (20.0%)	21 (30.9%)	5 (12.8%)	0.07
Gestational age of 37 weeks	23 (28.7%)	36 (52.9%)	16 (41.0%)	0.01
Maternal obesity	25 (31.2%)	26 (38.2%)	10 (25.6%)	0.38
Male sex	42 (52.5%)	34 (50.0%)	19 (48.7%)	0.91
Smoking / Illicit drug use	10 (12.5%)	9 (13.2%)	4 (10.3%)	0.90
Previous child requiring phototherapy ^a	8 (17.8%)	5 (16.1%)	2 (12.5%)	0.88
Maternal race (Asian)	1 (1.2%)	1 (1.5%)	0 (0.0%)	0.75

^an: 92. Multiparous patients whose other children may have required phototherapy. Pearson's chi-square test.

Source: The authors.

Newborns with ABO blood group

incompatibility and Rh factor incompatibility developed jaundice and required phototherapy earlier than infants without incompatibility. In

addition, these infants required phototherapy for a longer period of time ($p < 0.001$) (Table 5).

Table 5 – Jaundice in infants with and without ABO group/Rhesus factor incompatibility (n = 187) in Curitiba, Paraná, Brazil (CHC-UFPR), 2023–2024

Maternal Characteristics	Without (n = 112)	With (n = 75)	p
Causes of Jaundice	38.5 + 1.3	38.8 + 1.2	0.07 ¹
Characteristics			
Gestational age (weeks)	32 (22–4,5)	20 (14–27)	< 0.001 ²
Onset of jaundice	11.9 + 2.7	9.2 + 2.3	< 0.001 ¹
Hours of life			
Total serum bilirubin (mg/dL)	51.5 (42–58.5)	28 (20–40)	< 0.001 ²
Initiation of phototherapy	13.8 + 2.6	10.2 + 2.6	< 0.001 ¹
Hours of life	55.0 + 6.0	48.1 + 6.6	< 0.001 ¹
Total serum bilirubin (mg/dL)	27 (24–48)	45 (26–68)	< 0.001 ²
Hematocrit (%)	19 (17.0%)	10 (13.3%)	0.64 ³

¹ Student's t-test ² Mann-Whitney test ³ Pearson's chi-square test with Yates' correction.
Source: The authors.

Exclusive breastfeeding was practiced in 171 (91.4%) infants at the onset of jaundice. Breastfeeding jaundice was identified as the cause of hyperbilirubinemia in 59 (31.6%) newborns, most of whom were born

vaginally (67.8%), at 37 weeks' gestation (52.5%) and were male (52.5%). Regarding maternal data for infants with breastfeeding jaundice, most were primiparous (52.5%), 39.0% were obese, and 30.5% had pre-existing or gestational diabetes.

DISCUSSION

Neonatal jaundice is one of the most common clinical conditions occurring during the transition period after birth, and phototherapy is a treatment option for some infants.^{1,2,4,5,13,18} In this study, the incidence of indirect hyperbilirubinemia requiring phototherapy in healthy term newborns was 6.8%. In other

studies, the incidence ranged from 3.6% to 17.6%.^{4,5,13,18}

The risk factors for neonatal hyperbilirubinemia are diverse, complex, and may be interrelated.^{5,6,7,12,15,19} Delayed umbilical cord clamping (59.9%) was the main factor associated with jaundice, which can be explained by the fact that our hospital follows the recommendation for delayed umbilical cord clamping in babies born with good vitality; in our study, the median time to umbilical cord clamping was 120 seconds.^{5,12} Some authors^{11,12,20} reported that delayed umbilical cord clamping increased the risk of jaundice requiring phototherapy, while others did not.^{21,22} Maternal age >25 years was found in 52.7% of cases, whereas Isa et al. showed that maternal age of 25 years or older was the most common factor (85.9%) for the development of neonatal indirect hyperbilirubinemia.² Norman et al. identified maternal age of 30 years or older as a risk factor for jaundice, and maternal age <20 years was associated with a lower risk of neonatal hyperbilirubinemia.¹⁷ Ayalew et al. reported that the probability of a newborn-born infant developing jaundice was 8.8 times higher in mothers over 35 years of age compared to those under 25 years of age.⁷ In our study, 49.2% of infants with jaundice were male, and in other studies the rate ranged from 44.3% to 53.3%.^{2,16,18} Ayalew et al.⁷ and Norman et al.¹⁷ identified a risk factor of 1.41 to 4.3 times higher for jaundice in male newborns compared to female newborns, while Yang et al.¹⁶ found no difference based on sex. ABO blood group incompatibility (44.9%) was the fourth associated factor identified in this study, whereas in the study by Isa et al.² it was the second risk factor found in 37.6% of cases.

Ayalew et al.⁷ found that newborns with ABO incompatibility were 2.6 times more likely to develop

jaundice compared to those without ABO incompatibility. Similarly, Lin et al.¹⁹ and Olusanya et al.²³ reported that ABO incompatibility is a risk factor for hyperbilirubinemia. In this study, infants <38 weeks of gestational age presented with jaundice more frequently, corresponding to the fifth associated factor with a frequency of 40.1%. Norman et al.¹⁷ found that newborns with a gestational age between 37 and 38 weeks had a 2.83-fold higher risk of developing jaundice than those older than 38 weeks. Weight loss occurred in 31.6% of our infants. Yang et al.¹⁶ found that newborns with a higher percentage of weight loss had higher bilirubin levels. Dias et al.¹³ showed that excessive weight loss increased the likelihood of these infants requiring phototherapy by 1.2 times. Some studies did not investigate excessive weight loss as a risk factor for jaundice. Our hospital is part of the Baby-Friendly Hospital Initiative, where we have a high rate of exclusive breastfeeding, and infant formula is not routinely introduced; it is used only in specific cases, such as hypoglycemia or when exclusive breastfeeding is contraindicated. It should be noted that excessive weight loss is a preventable condition that can lead to the development or worsening of neonatal jaundice. This finding highlights the importance of healthcare professionals' role in providing guidance and support for breastfeeding during the period of hospitalization in rooming-in.

Numerous causes of neonatal jaundice are described in the literature.^{1,2,3,6,8} In this study, ABO incompatibility was the most common cause of indirect hyperbilirubinemia, affecting 40.1% of newborns. As previously described, incompatibility is also one of the most important risk factors for neonatal jaundice. Tsujimae et al.⁹ reported ABO incompatibility (22%) as one of the

main causes of indirect hyperbilirubinemia with a known cause, as did Pasha et al.¹ (16.9%). The second cause in this study was breastfeeding jaundice, accounting for 31.6% of cases; Tsujimae et al.⁹ reported a rate of 36%, while Isa et al.² reported a rate of only 7.6%. Our hospital belongs to the Baby-Friendly Hospital Initiative network, and 91.4% of our infants were exclusively breastfed at the onset of jaundice. It should be emphasized that breastfeeding jaundice does not occur because of breastfeeding itself, but due to inadequate breastfeeding resulting from insufficient milk production and/or difficulties with breastfeeding

(such as difficulty with latching or sucking by the newborn), leading to caloric deprivation and consequently weight loss in the baby.^{6,15} In fact, Hudson et al. reported a lower rate of phototherapy in the hospital following adherence to the Baby-Friendly Hospital Initiative network.¹⁴ To reduce the risk of breastfeeding jaundice, breastfeeding should be initiated within the first hour of the newborn's life, on-demand breastfeeding should be encouraged, mothers experiencing difficulties should be assisted, and mothers with lower milk production should be advised to increase the frequency of breastfeeding.^{6,15} In this study, when analyzing infants with breastfeeding jaundice, we observed that most were born at 37 weeks and were male; furthermore, 39.0% of the mothers were obese and 30.5% had diabetes, which are risk factors for hyperbilirubinemia described in the literature.^{5,6,7,9,13} Furthermore, most of these newborns were born to primiparous mothers, who may experience a later onset of lactation.²⁴ Idiopathic jaundice occurred in 20.9% of our newborns. In contrast, Pasha et al.¹ and Tsujimae et al.¹⁰ reported that 29% of infants with jaundice had no identified cause.

In this study, when evaluating factors associated with jaundice compared to the groups of jaundice causes, maternal age >25 years was the associated factor found in the non-hemolytic jaundice group, a finding similar to that reported by Lee et al.²⁵, who noted that advanced maternal age was associated with a higher risk of nonhemolytic jaundice, as advanced maternal age may establish a plausible link between multiple causes of nonhemolytic jaundice. In the hemolytic jaundice group, however, 37-week-old infants were the least likely to present with jaundice, and this may have occurred because in this group of newborns the most common cause was breastfeeding jaundice.

When comparing the causes of jaundice across gestational age groups, a higher frequency of G6PD deficiency was observed among 40-week-old newborns, but this data should be interpreted with caution, as the low number of infants in our study with this diagnosis must be taken into account.

Studies^{6,10,15} have shown that infants with ABO or Rh incompatibility developed neonatal jaundice within the first 24 hours, and this occurs due to a hemolytic process in which indirect bilirubin levels rise more rapidly than in infants without incompatibility. Furthermore, these newborns with incompatibility required earlier and longer-term phototherapy.^{6,10,15}

In this study, jaundice was initially diagnosed at a median of 25 hours of life for the infants, whereas Tsujimae et al.⁹ and van der Geest et al.¹⁸ reported that the onset of jaundice in most newborns occurred between 24 and 48 hours after birth. Our study showed a median duration of phototherapy of 30 hours, while van der Geest et al.¹⁸ reported a median of 22 hours; however, they did not analyze the causes of jaundice, whereas in

this study the main cause was ABO incompatibility, where the hemolytic process is present and persists for a longer duration. Dias et al.¹³ identified a hospital stay of 79 ± 28 hours in newborns who required phototherapy, whereas in our infants the mean duration was 119 ± 35.9 hours; this can also be explained by the fact that the main cause of jaundice in our study was ABO incompatibility. These data highlight the importance of noting that the length of hospital stay for infants with neonatal hyperbilirubinemia who do not require phototherapy is much shorter.¹³

This study has some limitations because it lacks a control group (jaundice group without the need for phototherapy) and was conducted at a single tertiary hospital, which may reduce its external validity. Because there was no control group, it was not possible to perform multivariate analyses or identify the risk factors involved; we could only report the factors associated with indirect hyperbilirubinemia requiring phototherapy.

However, this study has strengths, as it included healthy term newborns in rooming-in at a tertiary hospital belonging to the Baby-Friendly Hospital Initiative network, which reflects the reality of other public healthcare services. The study identified the factors associated with and the causes of jaundice in term infants requiring phototherapy—factors that can be monitored from birth, such as umbilical cord clamping time, gestational age, ABO incompatibility, and infant weight loss.

CONCLUSION

The most common factors associated with the development of neonatal jaundice requiring phototherapy were delayed umbilical cord clamping (>60 s), maternal age >25 years, and male sex. The prevent-

able associated factor identified was weight loss, reinforcing the need for guidance and support regarding breastfeeding practices. The most common causes of neonatal indirect hyperbilirubinemia requiring phototherapy were ABO incompatibility, breastfeeding jaundice, and idiopathic jaundice. Early identification of risk factors and associated factors for neonatal indirect hyperbilirubinemia is important so that these infants can be monitored more closely. Furthermore, the cause of jaundice should be identified, and treatment with phototherapy should be initiated as early as possible when indicated to reduce the length of hospital stay for these infants and prevent potential complications of neonatal jaundice.

Further studies should be conducted to confirm our findings, including a control group and involving more institutions from the Baby-Friendly Hospital Initiative, since Brazilian policy promotes breastfeeding.

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