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ORIGINAL ARTICLE

Neonatal jaundice: risk factors associated with performing phototherapy in a rooming-in care setting

Vitória Silva Souza Dias Dias[1], Simone Manso de Carvalho Pelicia[2], José Eduardo Corrente[3], Ligia Maria Suppo de Souza Rugolo[3]

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Abstract

Objective: To investigate the frequency of neonatal jaundice and use of phototherapy, along with the risk factors associated with phototherapy in a rooming-in care (RC) setting. **Methods:** This retrospective study included newborns with gestational ages ≥ 35 weeks seen in an RC setting at a tertiary hospital between October and December 2017. The subjects were divided into two groups, each featuring newborns treated or not treated with phototherapy. All newborns with a gestational age ≥ 35 weeks without congenital anomalies seen in an RC setting were included. Subjects requiring admission to the neonatal ward were excluded. Clinical data relative to the mothers, pregnancies, newborns, and care practices were analyzed. Endpoint: use of phototherapy. Associations between groups were assessed via Student's t-test and the chi-squared test. Multiple logistic regression was employed to identify independent factors associated with the use of phototherapy. **Results:** Almost half (47%) of the 376 newborns included in the study developed jaundice, of which 66 (18%) were provided phototherapy. The treated group had a lower gestational age (38 vs. 39 weeks), higher umbilical cord bilirubin levels (2 vs. 1.5 mg/dL), greater weight loss (7 vs. 6%), greater incidence of ABO incompatibility (35 vs. 10%), and longer hospital stays (79 vs. 50 hours). Logistic regression found the following independent risk factors for phototherapy: gestational age (OR=6), umbilical cord bilirubin (OR=16), ABO incompatibility (OR=12), and weight loss (OR=1.24). **Conclusion:** Jaundice was a frequent finding in newborns on RC. Almost 20% of the newborns with jaundice unwere provided phototherapy. Weight loss was the only preventable risk factor for needing phototherapy. No protective factor was found.

[1] Júlio de Mesquita Filho São Paulo State University, Pediatrics Residency Program, School of Medicine of Botucatu - Botucatu - São Paulo - Brazil.
[2] Júlio de Mesquita Filho São Paulo State University, Pediatrics Department, School of Medicine of Botucatu - Botucatu - São Paulo - Brazil.
[3] Júlio de Mesquita Filho São Paulo State University, Biostatistics Department, Institute of Biosciences - Botucatu - São Paulo - Brazil.

Correspondence to:
Simone Manso de Carvalho Pelicia.
Universidade Estadual Paulista Júlio de Mesquita Filho. Av. Universitária, 3780 – Altos do Paraíso, Botucatu, SP, CEP: 18610-034. E-mail: carvalhomone@terra.com.br

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INTRODUCTION

Jaundice is a frequent complication in newborns, with incidence estimated at 50% in full-term and 80% in preterm neonates[1]. It is the clinical expression of hyperbilirubinemia, a condition that manifests when bilirubin levels exceed 4 to 6 mg/dL. Jaundice may be diagnosed based on the color of the skin of a newborn during physical examination using Kramer's scale, noninvasive transcutaneous bilirubinometry, or serum bilirubin levels[2-6].

Physiological jaundice, characterized by mild increases in bilirubin levels and commonly seen in healthy newborns within the first days of birth, usually does not call for the prescription of phototherapy. However, the need for phototherapy increases in hemolytic jaundice mainly due to ABO or Rh incompatibility, G_6PD deficiency, or other causes of hemolysis. Bilirubin levels also increase in the presence of risk factors for severe hyperbilirubinemia, such as prematurity, history of a sibling with neonatal jaundice, Asian ethnicity, significant cephalohematoma or birth injury, exclusive breastfeeding, induction of labor with oxytocin, delayed passage of meconium, and maternal diabetes[3,5,7,8].

Phototherapy is the method of choice in the treatment of jaundice. Devices currently used in phototherapy are extremely effective[9]. The frequency of use of phototherapy in a rooming-in care (RC) setting varies and is affected by multiple factors, such as the performance of screening tests, the risk profile of each newborn, and the guidelines used in prescription[10]. A recent study conducted at six tertiary referral hospitals in the United States that adopted the guidelines of the American Academy of Pediatrics (AAP) found that phototherapy was prescribed to 7% of newborns, all of which were healthy and with gestational ages ≥ 35 weeks[11]. At a low risk maternity hospital in Norway, phototherapy was deemed necessary only for 3.1% of newborns as per local guidelines, while in Nigeria 5.9% of newborns qualified for phototherapy based on widely adopted international guidelines[10].

Phototherapy is a safe procedure with rare reports of adverse effects[7,10]. However, length of hospitalization increases when it is used on newborns on RC. The current RC standards dictate that discharge should occur 48 hours after delivery, which generates concerns over the undertreatment of jaundice and the possibility of onset of bilirubin encephalopathy, a severe complication derived from high bilirubin levels that may cause permanent neurologic sequelae, thereby compromising the prognosis of newborns[7,12]. Thus, it might be worth predicting which newborns are in greater need of phototherapy and, more importantly, identify preventable risk factors and protective factors alike. This study aimed to assess the frequency of occurrence of jaundice and the use of phototherapy in newborns on RC seen at a tertiary hospital, and to investigate the factors associated with need of phototherapy.

METHOD

This retrospective study included newborns on RC seen at a tertiary hospital from October to December 2017.

The institution's Research Ethics Committee approved the study (certificate no. 3.748.815) and the guardians of the infants seen in the outpatient ward signed informed consent terms.

All newborns with a gestational age ≥ 35 weeks on RC at the hospital were included. Newborns with congenital anomalies and the ones that were transferred to the neonatal ward were excluded.

The following data related to the mothers and pregnancies were reviewed: age, parity, gestational diseases (diabetes mellitus, chronic hypertension, gestational hypertension, preeclampsia), drug use, smoking, alcohol drinking, and type of delivery.

The following newborn-related variables were reviewed: gestational age (calculated based on the best obstetric estimate: early-stage US or precise date of last period), birth weight, weight for gestational age (based on the criteria published by Fenton and Kim, 2013), sex, need for positive pressure ventilation with a balloon and bag valve mask at birth, 1- and 5-minute APGAR scores, presence of ABO or Rh incompatibility, G6PD deficiency, total umbilical cord bilirubin, maximum total bilirubin, weight on second day of life, percent weight loss on second day of life, weight at discharge, length of hospital stay[13].

The following care practices were reviewed: length of umbilical cord clamping, skin-to-skin contact, breastfeeding within the first hour of birth, and exclusive breastfeeding.

The protocols in effect for the assessment of jaundice at our service stipulate that umbilical cord bilirubin levels be measured at birth and a clinical assessment of the newborn performed within 6-12 hours of birth and daily during hospitalization. Newborns with umbilical cord bilirubin levels ≥ 4 mg/dL also have serum levels tested (serum bilirubin, complete blood count, reticulocytes) and are started on phototherapy until test results are available. Two members of the RC medical team assess the clinical status of newborns based on Kramer's scale, one of them the attending physician. When jaundice advances onto dermal zone 2 within 24 hours or zone 3 within 24-48 hours of birth, bilirubin levels are measured with a Bilicheck transcutaneous bilirubinometer[4]. When the levels read on the Bilicheck are greater than 12 mg/dL, serum bilirubin is measured. In cases of early jaundice, a sample of blood is collected and tested for bilirubin and other markers of hemolysis. Such as reticulocytes, hemoglobin, and hematocrit. Patients are prescribed phototherapy as indicated in the curve proposed by the AAP in 2004 for full-term and late preterm newborns (neonates born with gestational ages ranging from 34 weeks and one day and 36 weeks and six days)[6,14].

In our study, patients were stratified into two groups: Treated Patients (newborns given phototherapy) and Untreated Patients (newborns not given phototherapy).

Associations between groups were assessed based on Student's t-test for continuous variables or the chi-squared test for categorical variables. Variables with differences in univariate analysis expressed by p-values < 0.05 in the chi-squared test were submitted to multiple logistic regression analysis to identify independent factors associated with use of phototherapy. Statistical significance was attributed to differences with a $p < 0.05$ and the odds ratios used came from the adjusted model without correction.

RESULTS

A total of 448 newborns stayed on RC and 376 met the inclusion criteria. From this number, 176 (46.8%) developed jaundice. Sixty-six newborns (17.6%) required phototherapy. The treated group contained 66 newborns and the untreated group 310. Figure 1 shows the study design flowchart.

Patients born in October-December 2017 n=565 | Patients on RC n=448 | 72 excluded | Included n=376 | Without jaundice n=200 | With jaundice n=176 | Treated n=66 | Untreated n=110 || Referred to high/medium risk unit n=117 | 4 with malformations 68 referred to high/medium risk unit

When maternal variables were considered, only gestational hypertension and vaginal delivery were different between groups (Table 1). Fewer cases of gestational hypertension (3.0% vs. 14.5%; p = 0.010) and a greater proportion of vaginal deliveries (77% vs. 61%; p = 0.011) were observed in the treated group.

The included newborns had good vitality levels at birth and scored 9 in the 1-minute Apgar test on average. One newborn had Rh incompatibility; this newborn did not require phototherapy. None of the newborns had G6PD deficiency. The main data collected from the included newborns and the identified significant differences are shown in Table 2. Care practices did not differ between groups (Table 3).

All variables with a significant difference ($p < 0.05$) between groups in bivariate analysis, except for length of hospitalization, and variables without a significant difference associated with need for phototherapy, such as male sex and length of cord clamping, were included in multivariate analysis with logistic regression. This analysis allowed the identification of a number of independent risk factors and no protective factor associated with need for phototherapy (Table 4).

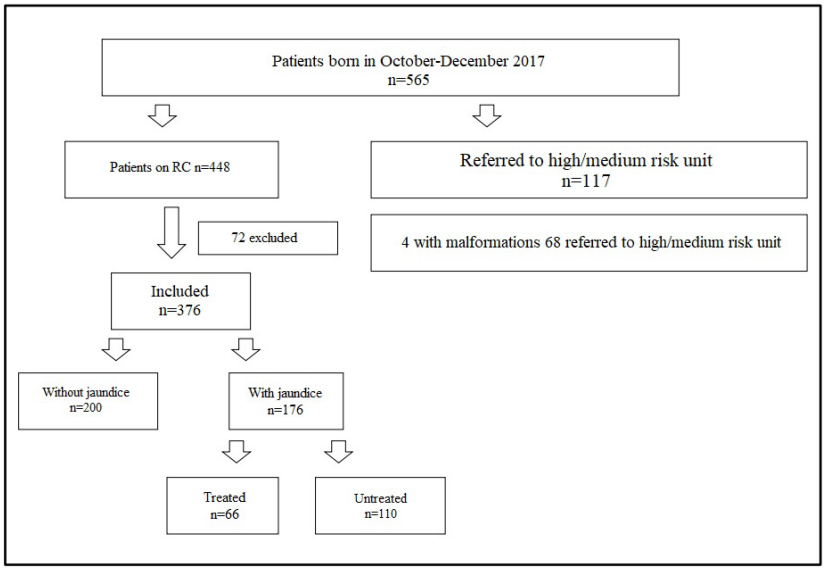

Figure 1. Study design flowchart
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Table 1. Maternal and pregnancy-related data from treated and untreated newborns

Variable	Treated (n=66)	Untreated (n=310)	p-value
Age (years) ± SD	27 ± 7	26 ± 6	0.069
First pregnancy (%)	20 (30)	103(33)	0.646
Chronic hypertension (%)	4 (6)	13 (4)	0.507
Gestational hypertension (%)	2 (3)	45(14.5)	0.010
Preeclampsia (%)	2 (3)	21(6.5)	0.249
Diabetes (%)	5(7)	26(8.5)	0.828
Drug use (%)	2(3)	4(1.3)	0.306
Smoking (%)	10(15)	37(12)	0.473a
Alcohol drinking (%)	4(6)	12(4)	0.424
Vaginal delivery (%)	51(77)	188(61)	0.011

* SD= standard deviation

Table 2. Data from treated and untreated newborns

Variable	Treated (n=66)	Untreated (n=310)	p-value
GA (weeks) mean ± SD	38 ± 1.4	39 ± 1.2	< 0.001
GA < 37 weeks (%)	12(20)	13(4.5)	< 0.001
BW (g) mean ± SD	3200 ± 390	3235 ± 420	0.530
Adequate weight for GA (%)	59(89.5)	267(86)	0.610
Male sex (%)	33(50)	149(48)	0.881
Need of resuscitation (%)	3(5)	29(9)	0.214
ABO incompatibility (%)	23(35)	31(10)	< 0.001
Umbilical cord TB (mg/dL) mean ± SD	2 ± 0.6	1.5 ± 0.4	< 0.001
Jaundice < 24 hours of birth (%)	9(13)	0(0)	< 0.001
Maximum TB (mg/dL) mean ± SD	10.5 ± 2.1	8.8 ± 1.4	< 0.001
Weight on Day 2 after birth (g) mean ± DP	2980 ± 345	3035 ± 390	0.261
%↓ weight loss on Day 2 ± SD	7 ± 2	6 ± 2	0.017
Weight (g) at discharge mean ± SD	2995 ± 350	3040 ± 385	0.376
Length of hospitalization (h) ± SD	79 ± 28	50 ± 20	< 0.001

*GA= gestational age; SD= standard deviation; BW= birth weight; g=grams; TB= total bilirubin; h= hours

Table 3. Care practices for treated and untreated newborns

Variable	Treated (n=66)	Untreated (n=310)	p-value
Cord clamping > 2 min (%)	31(48)	158(51)	0.411
Skin-to-skin contact (%)	27(41)	118(38)	0.631
Breastfeeding within one hour of birth (%)	59(89)	247(80)	0.079
Exclusive breastfeeding (%)	59(89)	281(91)	0.754

Table 4. Risk factors associated with need of phototherapy

Variable	*Odds ratio** (95% CI)
Gestational age < 37 weeks	6.0 (1.8 - 19.4)
Umbilical cord bilirubin (each 1 mg/dL)	16.6 (6.3 - 43.5)
ABO incompatibility	12.3 (4.6 - 32.7)
Weight loss (each 1%)	1.2 (1.1 - 1.5)

* *Odds ratio* adjusted model without correction

DISCUSSION

Jaundice is one of the most common complications seen in neonates, which, although primarily benign, may damage the nervous system of newborns and cause long-term sequelae. The prevalence of jaundice in this study was 46.8%, a proportion similar to the ones published in the literature, with numbers in the 50% range for full-term newborns and up to 80% in late preterm infants, showing the importance of assessing, diagnosing, and properly treating individuals with neonatal jaundice to prevent complications associated with hyperbilirubinemia[1,3,7].

A noteworthy finding was the use of phototherapy in almost 20% of the newborns on RC, against proportions below 10% described in the literature for full-term healthy newborns or late preterm babies[10,11]. The difference may be partly due to the fact that this study was carried out at a teaching hospital, in which standard criteria and protocols are used in the assessment and treatment of newborns on RC with jaundice. Different methods and screening tests for hyperbilirubinemia and differences between treatment guidelines affect the prescription of phototherapy[10]. It is important to note that the prescription of phototherapy led to longer hospitalization (79 vs. 50 hours), which increases healthcare costs and anxiety levels of parents and families[15,16,17].

Jaundice in newborns is influenced by multiple factors, including maternal diabetes, ethnicity, use of medication by the mother, prematurity, male sex, cephalohematoma, breastfeeding, weight loss, and delayed passage of meconium[3,7].

The association between type of delivery and neonatal jaundice has been the subject of controversy, with studies documenting an association between vaginal delivery and increases or decreases in the incidence of jaundice[18,19]. Such discrepancy is possibly due to confounding factors involved in the choice of a specific mode of delivery and the use of oxytocin in the induction of labor, prolonged labor, and greater incidence of cephalohematoma in vaginal deliveries, which increase the risk of neonatal hyperbilirubinemia[3,20].

In our study, vaginal delivery was more prevalent in the group that needed phototherapy, although we have not looked into the factors that might justify this finding.

Our results did not show any impact from maternal factors, although gestational hypertension was more frequent in the group that did not require phototherapy. This finding contradicted the results reported in a previous study, in which hypertension was identified as a risk factor for hyperbilirubinemia due to an association with preterm birth[21]. Our study included newborns on RC. Therefore, since we had fewer cases of maternal disease. Likewise, fewer repercussions from such diseases were expected to affect the included newborns, who were either full-term or close to full-term and healthy at birth.

ABO incompatibility was an important risk factor associated with a 12-fold increase in need of phototherapy. This finding was somewhat expected, since hemolytic disease in newborns causes a rapid increase in bilirubin levels[8]. Knowledge of the blood type of mothers and their children may help identify newborns at greater risk of developing jaundice and provide them with early treatment for the condition.

Our study showed that having an elevated umbilical cord bilirubin level is a risk factor for needing phototherapy. A study with 1411 full-term newborns revealed that umbilical cord bilirubin levels of infants born to mothers with O-type blood predicted the incidence of jaundice, a useful strategy in the early identification of newborns at risk of hemolytic jaundice[22]. Our study extended the use of umbilical cord bilirubin levels and found that higher levels increase the chances of a newborn developing jaundice and require phototherapy, regardless of the presence of hemolytic disease.

Late preterm newborns on RC had a six-fold increase in the chance of needing phototherapy. This finding is in agreement with the literature and serves as a reminder of the care this group of newborns requires, which is typically the same care provided to full-term infants despite their four-fold chance of developing a morbid condition[23]. In addition to occurring more frequently, jaundice is more severe in late preterm newborns on account of several factors, including the shorter half-life of red blood cells, lower hepatic uptake and conjugation of bilirubin, and increased enterohepatic circulation due to immaturity of the gastrointestinal tract, the latter potentially exacerbated by difficulty feeding a newborn. Late preterm newborns are more prone to developing feeding difficulties and require closer attention when breastfed, along with advice to mothers about potentially increasing the frequency of nursing[23]. In late preterm newborns, phototherapy is a frequent cause of readmission, as described by Punaro et al., who reported prescription of phototherapy to 18.9% of previously discharged newborns with gestational ages of 35-37 weeks[24].

The most important finding of the study was the identification of a preventable risk factor for jaundice requiring phototherapy: weight loss within the first days after birth. This is a warning against providing insufficient nourishment to newborns within the first days of birth, a factor that contributes to increased occurrence of jaundice. Healthcare workers involved in newborn care must actively engage their mothers and provide them with advice and support about breastfeeding throughout their stay on RC. Encouraging and supporting breastfeeding are good care practices and may produce a positive impact on weight loss in the days immediately after birth and prevent the need for phototherapy in newborns on RC[25].

Our study has its limitations, since it is a retrospective analysis that included patients seen at a tertiary hospital in which high risk individuals are treated, which may diminish its external validity. Given its retrospective nature, it analyzed data collected from routine care records and newborn patient charts. Some risk factors for jaundice such as ethnicity, birth injury, use of oxytocin, history of a sibling that needed phototherapy, and delayed passage of meconium were not considered for lack of information about them.

Nonetheless, the study also has its strengths. It looked into the situation of newborns on RC, i.e., healthy newborns, thus reflecting the reality of other public services. The analysis of the studied population allowed the identification of risk factors tied to the need of phototherapy among newborns on RC, and elements that can be watched from birth, such as prematurity, ABO incompatibility, and umbilical cord bilirubin. Weight loss was also identified as a preventable risk factor. This knowledge may contribute to improve clinical practice and the care provided to newborns on RC.

Additional studies are required to confirm our findings and assess newborns referred to neonatal wards, since they might present more risk factors.

In conclusion, jaundice is a frequent finding in newborns in a rooming-in care setting, with almost 20% requiring phototherapy. Although numerous risk factors for need of phototherapy were found, weight loss was the only preventable element, thereby stressing the need to look at breastfeeding with utter caution. No protective factor was found.

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