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ASSOCIATED FACTORS WITH JAUNDICE REQUIRING PHOTOTHERAPY: A CASE-CONTROL STUDY IN A HOSPITAL IN PERU

FACTORES ASOCIADOS A ICTERICIA CON REQUERIMIENTO DE FOTOTERAPIA: ESTUDIO DE TIPO CASOS Y CONTROLES EN UN HOSPITAL DE PERÚ

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ABSTRACT

Objective: The aim was to identify the factors linked to jaundice that necessitates phototherapy. **Methods:** An observational, analytical, and retrospective case-control study was conducted. The medical records of 212 patients aged 0 to 7 days from the neonatology service at Hospital Carlos Lanfranco La Hoz were reviewed, divided into 106 cases (with phototherapy) and 106 controls (without phototherapy). **Results:** Preterm neonates showed a significant association with an OR: 5.526; 95% CI (2.038-14.981), P= 0.001; and ABO incompatibility had an OR: 4.373, 95% CI (1.934-9.889), P= 0.001. **Conclusions:** The study concludes an association between preterm neonates, ABO incompatibility, and the necessity for phototherapy.

Keywords: Jaundice neonatal; Risk factors; Phototherapy. (Source: MESH-NLM)

RESUMEN

Objetivo: Determinar los factores asociados a ictericia con requerimiento de fototerapia. **Métodos:** Estudio observacional, analítico, y retrospectivo de tipo casos y controles. Se revisaron las historias clínicas de 212 pacientes de 0 a 7 días de nacidos del servicio de neonatología del Hospital Carlos Lanfranco La Hoz, divididos en 106 casos (con fototerapia) y 106 controles (sin fototerapia). **Resultados:** Se encontró una asociación significativa entre los neonatos pretérmino y la necesidad de fototerapia, con un OR:5.526; IC 95% (2.038-14.981), P= 0.001; así como una asociación entre la incompatibilidad ABO y la fototerapia, con un OR:4.373, IC 95% (1.934-9.889), P= 0.001. **Conclusiones:** Se concluye que existe asociación entre neonatos pretérmino, la incompatibilidad ABO con la necesidad de fototerapia.

Palabras clave: Ictericia neonatal; Factores de riesgo; Fototerapia. (Fuente: DeCS- BIREME)

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INTRODUCTION

Jaundice is the most common clinical sign in neonates and is often the reason for readmissions and admissions to Intermediate Care Units (IMCU) to receive phototherapy. It occurs in 50-60% of term neonates and close to 80% of preterm infants. Of these, 20% require phototherapy to prevent complications such as encephalopathy and Kernicterus⁽¹⁾.

A study in the United States on hospitalizations for jaundice and Kernicterus revealed a decrease in Kernicterus cases and related hospitalizations. However, between 1988 and 2005, the trend of hospitalized neonates with jaundice was still 15.6%⁽²⁾. A meta-analysis revealed that the rate of severe neonatal jaundice is significantly higher in Africa, with 667.8 cases per 10,000 live births, compared to Europe, which has an incidence of 3.7 per 10,000 live births⁽³⁾. In Peru, the incidence of neonatal jaundice is 39 per 1000 live births, with Lima and Callao accounting for 48% of cases, while the regions of Cusco, Arequipa, La Libertad, and Ica have the highest incidence rates⁽⁴⁾.

Jaundice is the seventh leading cause of neonatal mortality worldwide, with a rate of 1306.3 per 100,000 live births, highlighting the importance of timely management⁽⁵⁾. Two types of hyperbilirubinemia are distinguished: physiological and pathological, and it is crucial to identify their possible causes, such as hemolysis, infections, and obstetric complications⁽⁶⁾. Phototherapy is the first-line treatment for hyperbilirubinemia. However, it is important to note that some studies mention its association with allergic diseases after its use, such as asthma, allergic rhinitis, atopic dermatitis, and even food allergies⁽⁷⁾. According to a study in California, USA, 8% of 50,000 newborns received this treatment⁽⁷⁾.

In Peru, studies have been conducted on factors associated with neonatal jaundice. However, this research aims to highlight the importance of neonates requiring phototherapy in intermediate care and analyze the maternal-neonatal conditions that affect their length of stay. It also aims to identify strategies to reduce admission to the neonatal IMCU. Therefore, this study sought to determine the factors associated with

jaundice requiring phototherapy at Hospital Carlos Lanfranco La Hoz during the period 2021-2022.

Design and Study Area

Observational, analytical, retrospective case-control study.

Population and Sample

The study population consisted of 212 neonatal patients aged 0-7 days, with gestational ages between 35 and 41 weeks, diagnosed with jaundice. These patients were divided into two groups: 106 cases (required phototherapy) and 106 controls (did not require phototherapy). Neonates with congenital malformations were excluded.

Variables and Instruments

The main variable was: Jaundice requiring phototherapy. The independent variables analyzed were: gestational age, birth weight, ABO incompatibility, Rh incompatibility, neonatal sepsis, maternal Urinary Tract Infection (UTI), and maternal anemia.

Procedures

To collect information on neonatal jaundice, both in cases requiring phototherapy and those without, the technique of reviewing medical records was used. These records collected data from both the neonate and the mother, who were treated in the neonatology hospitalization service of Hospital Carlos Lanfranco La Hoz during the period from 2021 to 2022, according to the established objectives. Subsequently, the collected data were entered into the Microsoft Excel 2019 program, and the corresponding analyses were performed using the IBM SPSS v29 program.

Statistical Analysis

A database was extracted from a data collection form and recorded in Microsoft Excel 2019. It was then processed in IBM SPSS v29 for statistical analysis. Qualitative variables were described using frequencies and percentages, while quantitative variables were evaluated for normality, and measures of central tendency and dispersion were calculated. To identify





factors associated with neonatal jaundice requiring phototherapy, a bivariate analysis was performed using the chi-square test, considering a significance level of $p < 0.05$ and a confidence interval of 95%. The Odds Ratio (OR) measure of association was also used. For the multivariate analysis, the adjusted Odds Ratio measure of association was used, considering a significance level of $p < 0.05$.

Ethical Aspects

The study followed current ethical standards and received approval from the Ethics Committee of the Universidad Ricardo Palma and the Hospital Carlos Lanfranco La Hoz. The proper use of data and research ethics were guaranteed, maintaining the integrity and confidentiality of the participants' medical records. Since the information was obtained from the review of medical records, specific informed consent was not used for this study.

RESULTS

The research covered 212 medical records of neonates diagnosed with neonatal jaundice, divided into two groups: 106 neonates requiring phototherapy (cases) and 106 neonates not needing phototherapy (controls). The mean gestational age for the entire sample was 38.26 weeks, and the mean birth weight was 3213g. In the univariate analysis (see Table 1), it was observed that 25.5% of neonates in the case group were preterm, and 74.5% were term.

Regarding weight, 18.9% had low birth weight, 72.6% had adequate weight, and 8.5% were macrosomic. It was also found that 30.2% of neonates in the case group had ABO incompatibility, and only 0.1% with Rh incompatibility required phototherapy. 7.5% of cases had a positive diagnosis of neonatal sepsis, while 24.5% had maternal UTI, and 17% had a history of maternal anemia (Table 1).

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Table 1. Frequency distribution of independent variables.

Variable	Categories	Case		Control	
		N	%	N	%
Gestational Age	Preterm	27	25.5	6	5.7
	Term	79	74.5	100	94.3
Birth weight	Low weight	20	18.9	6	5.7
	Macrosomic	9	8.5	14	13.2
ABO Incompatibility	Adequate	77	72.6	86	81.1
	Yes	32	30.2	11	10.4
Rh Incompatibility Rh	No	74	69.8	95	89.6
	Yes	1	0.9	1	0.9
Neonatal sepsis	No	105	99.1	105	99.1
	Yes	8	7.5	8	7.5
Maternal UTI	No	98	92.5	98	92.5
	Yes	26	24.5	17	16
Maternal Anemia	No	80	75.5	89	84
	Yes	18	17	17	16
	No	88	83	89	84
Total		106	100	106	100

Source: Own elaboration.



In the bivariate analysis, a significant difference was found in the risk of needing phototherapy according to gestational age, with preterm neonates being 5.96 times more likely to require it than term neonates. Birth weight also showed statistical significance, with low-birth-weight neonates having 73.1% fewer chances of needing phototherapy. However, macrosomic

neonates did not show a solid association. ABO incompatibility showed a significant association, with neonates with a positive diagnosis being 3.73 times more likely to require phototherapy than those without ABO incompatibility. The other variables analyzed did not show a statistically significant association (Table 2).

Table 2. Bivariate analysis of risk factors associated with the need for phototherapy in the neonatology service of Hospital Carlos Lanfranco La Hoz.

Variable	Categories	P Value	Crude OR	95% confidence interval of crude OR	
				Lower	Upper
Gestational weight	Preterm	0.001	5.96	2.242	14.473
	Term		Ref.		
Birth weight	Low weight	0.007	0.269	0.103	0.703
	Macrosomic	0.467	1.393	0.571	3.399
Adequate	Ref.				
ABO Incompatibility	Yes	0.001	3.73	1.765	7.902
	No		Ref.		
Rh Incompatibility	Yes	1	1	0.062	16.199
	No		Ref.		
Neonatal sepsis	Yes	1	1	0.361	2.771
	No		Ref.		
Maternal UTI	Yes	0.124	1.70	0.86	3.365
	No		Ref.		
Maternal anemia	Yes	0.853	1.07	0.518	2.212
	No		Ref.		

Source: Own elaboration.

In the multivariate analysis, gestational age and the presence of ABO incompatibility continued to show statistical significance. Preterm neonates were 5.52 times more likely to need phototherapy compared to

term neonates, and neonates with ABO incompatibility were 4.37 times more likely to require it compared to those without the diagnosis. However, birth weight lost significance in the multivariate analysis (refer to Table 3).

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Table 3. Multivariate analysis of risk factors associated with the need for phototherapy in the neonatology service of Hospital Carlos Lanfranco La Hoz.

Variable	Categories	P Value	Adjusted OR	95% confidence interval of Adjusted OR	
				Lower	Upper
Gestational Age	Preterm	0.001	5.526	2.038	14.981
	Term		Ref.		
Birth weight	Low weight	0.086	0.394	0.137	1.139
	Macrosomic	0.670	1.230	0.474	3.192
ABO Incompatibility	Adequate		Ref.		
	Yes	0.001	4.373	1.934	9.889
Rh Incompatibility	No		Ref.		
	Yes	0.910	0.837	0.038	18.184
Neonatal sepsis	No		Ref.		
	Yes	0.718	1.227	0.405	3.724
Maternal UTI	No		Ref.		
	Yes	0.252	1.554	0.731	3.303
Maternal Anemia	No		Ref.		
	Yes	0.773	0.887	0.391	2.008

Source: Own elaboration.

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DISCUSSION

Main Findings

In our study, statistically significant factors associated with neonatal jaundice requiring phototherapy were identified, including a gestational age of less than 37 weeks and the presence of ABO incompatibility. The lack of statistically significant results related to jaundice and Rh incompatibility may be attributed to the low incidence of Rh incompatibility in our sample. With only 2 neonates out of 212 cases presenting Rh incompatibility, the scarcity of cases limits our ability to detect a significant association between Rh incompatibility and jaundice in this study.

Comparison with other studies

This study analyzed a sample in which 15.5% of neonates were born prematurely (<37 weeks), and within this group, 25.5% required phototherapy.

The results revealed a statistically significant relationship with a value of $p=0.001$ and an $OR=5.52$. These findings coincide with those of Amable O., who also found a statistically significant association between prematurity and the need for phototherapy, with an $OR=2.98$ and a value of $p<0.001$. Another study conducted by Meza P. supports these results, demonstrating a significant association between prematurity and phototherapy, with an $OR=2.03$ and a value of $p<0.015$. However, there is a study in Brazil, conducted by Dias V. et al., where it was observed that term neonates had a greater association with the need for phototherapy. In this study, gestational age ranged between 38 and 39 weeks⁽⁸⁻¹⁰⁾.

This is explained because late preterm newborns (34 0/7-36 6/7 weeks of gestation) show a decrease in UGT1A1 enzyme activity, which affects bilirubin clearance, prolonging jaundice.





Additionally, they may have difficulties in the feeding behavior and suckling reflex, which can lead to poor breastfeeding⁽¹¹⁾.

Several previous studies have observed an association between ABO incompatibility and the requirement for phototherapy in newborns. For instance, a strong association between both variables was found in studies conducted by Dias V. and Avalos M., with OR=12 and OR=24 respectively. Another study in Huancayo, a highlander city of Perú, found a statistically significant association with OR=1.21. In our research, a significant association was also found between ABO incompatibility and the need for phototherapy, with an OR=4.37 and a p-value of 0.001^(10,12,13).

We know that jaundice due to ABO incompatibility is caused by hemolysis and occurs in around 20% of pregnancies, where the presentation is usually O-B or O-A^(11,14). These results support the idea of a strong association between ABO incompatibility and the need for phototherapy in newborns. Low birth weight and macrosomia are risk factors for developing neonatal jaundice. In the study, it was found that 18.9% of newborns with low birth weight, 8.5% of macrosomic newborns, and 72.6% of newborns with adequate weight required phototherapy. In the bivariate analysis, low birth weight was significant and acted as a protective factor with an OR=0.269 and a p-value of 0.007.

However, in the multivariate analysis, this relationship lost statistical significance (OR=0.394; p=0.086), probably due to the sample size of the hospital. These results are consistent with similar studies conducted by Dias V. and Meza P., where no statistically significant association was found between birth weight and phototherapy. In contrast, another study conducted by Amable O. showed a strong association between low birth weight and jaundice requiring phototherapy, with a p-value of 0.001 and an OR=3.26, and a higher presentation frequency of 41.7%^(15,6,7). Low birth weight can alter the blood-brain barrier and increase the risk of

Kernicterus. In the case of macrosomic newborns, higher body weight can lead to increased bilirubin formation, as bilirubin formation per day can range between 8-10mg per kilogram of weight, increasing the risk of hyperbilirubinemia⁽¹⁵⁾.

Recommendations

It is recommended to investigate variables such as the history of phototherapy in siblings or parents, but these could not be studied due to the lack of registration in medical records. Additionally, proper breastfeeding technique is another variable of interest, but its complete evaluation was limited by the absence of periodic assessments during hospitalization, which could introduce biases.

A prospective study is suggested to determine if neonates who received phototherapy developed allergic diseases such as asthma, atopic dermatitis, or allergic rhinitis. Further studies on possible rebound cases after phototherapy treatment are also recommended. Variables such as gestational age less than 37 weeks, neonatal sepsis, early onset of phototherapy, and hemolytic diseases should be considered, as they could be causes of hospital readmissions.

Limitations

Difficulty in finding cases that met the inclusion criteria.

CONCLUSIONS

The factors associated with the need for phototherapy were prematurity and ABO incompatibility. It is of utmost importance to recognize the risk factors, to treat them preemptively in order to avoid complications, and also to improve the health and quality of life of newborns. Additionally, surveillance and guidance to mothers during the gestation period and hospitalization in rooming-in are recommended since there are other influential factors in the development of jaundice.





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