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Relationship between Neonatal Skin Bilirubin Level and Severe Jaundice with Maternal, Childbirth, and Neonatal Characteristics

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ABSTRACT

Background: Neonatal jaundice is the most common cause of newborns' hospitalization. This study aimed to examine various maternal, childbirth, and neonatal factors affecting the neonatal skin bilirubin level and severe jaundice.
Methods: This cross-sectional study was conducted on 1066 healthy neonates with a gestational age of 35 weeks or over and birth weight of ≥2000 g at teaching hospitals of Alzahra and Taleghani in Tabriz, Iran, during 2016-2017. The participants were selected using convenience sampling. Data were collected using a three-part researcher-made questionnaire assessing maternal, childbirth, and neonatal characteristics based on the medical histories of mothers and newborns as well as interviews with mothers. Neonatal jaundice was measured utilizing the Kj-8000 device on days 3-6 after birth by measuring the skin bilirubin level. Moreover, the need to phototherapy (severe jaundice) was determined based on the American Academy of Pediatrics guideline. The generalized linear model and multivariate logistic regression were employed for data analysis.
Results: Out of the followed-up neonates, 94 (9.96%) cases developed severe jaundice and 850 (90.04%) newborns did not show any symptoms of this complication. The results of the adjusted generalized linear model showed that infant's bilirubin level correlated significantly with a history of jaundice in previous children, infant's age at first meconium excretion, frequency of feeding, gestational age, mother's blood type, and a number of maternal ultrasound during pregnancy. Moreover, the results of adjusted logistic regression revealed an association between severe jaundice and variables, such as the place of residence, history of jaundice in previous children, feeding the infant with water or sugar water during breastfeeding intervals, frequency of feeding the infant, gestational age, mother's blood type, time of discharge from the hospital, and number of pregnancies.
Conclusion: Some factors related to neonatal jaundice were identified to raise the awareness of healthcare personnel for the early identification and treatment of neonatal jaundice in order to prevent its complications.

Keywords: Jaundice, Risk Factor, Transcutaneous bilirubin

Introduction

Reduction of neonatal mortality and identification of preventable factors which lead to the rehospitalization of neonates are of utmost importance globally (1). Jaundice is the most common cause of newborn' hospitalization in the first month after birth. More than half of term neonates and four-fifths of premature newborns who are otherwise healthy develop a degree of jaundice two to five days after birth (2). Hyperbilirubinemia occurs in over 60% of term and near-term and 80% of preterm neonates as a common finding in the first days of birth (3).

Based on previous studies, the major risk factors of severe hyperbilirubinemia in neonates

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with 35 weeks or more of gestational age include level of transcutaneous bilirubinometry (TCB) or total serum bilirubin (TSB) in the high-risk zone (based on the Bhutani Nomogram) before discharge, jaundice in the first 24 hours of birth, blood type incompatibility together with the positive direct antiglobulin test, other known hemolytic diseases, increased carbon monoxide in the tidal volume, gestational age of 35-36 weeks (4), history of phototherapy on previous children (5), cephalohematoma or severe bruising, exclusive breastfeeding, especially when breastfeeding is not performed properly, and severe loss of weight in the infant (6).

The minor risk-factors of this complication include the level of TSB or TCB in the intermediate-risk zone before discharge, gestational age of 37-38 weeks, observed jaundice before discharge, history of jaundice in previous siblings, neonates with macrosomia from mothers with diabetes (7), maternal age of 25 years or above, and male gender (5). Moreover, factors reducing the risk of hyperbilirubinemia are level of TSB and TCB in the low-risk zone, gestational age of 41 weeks or more, exclusive formula feeding, black race, discharge after 72 hours (5), and the initiation of feeding immediately after childbirth, especially in the first hour (8).

Jaundice is transient and self-limiting in most cases; however, it causes bilirubin encephalopathy and severe brain damage unless it is diagnosed timely and not being severed (9). The importance of preventing neonatal jaundice is probably more than that of its timely diagnosis and treatment. This, of course, requires the identification of jaundice risk-factors (10). Although various studies have been conducted on this domain in Iran (11-15), there is a need for further studies considering the importance and high prevalence of jaundice in this country. Therefore, the present cross-sectional study aimed to identify maternal, childbirth, and neonatal factors related to neonatal skin bilirubin level and severe jaundice.

Methods

Study design and participants

This cross-sectional study was conducted on 1066 healthy neonates with a gestational age of 35 weeks and over based on the last menstrual period (LMP), and if the LMP was unknown, based on the first ultrasound, and a birth weight of ≥2000 g at teaching hospitals of Alzahra and Taleghani in Tabriz, Iran, during 2016-2017. The neonates with major congenital defects, those admitted to intensive care units, those with mothers who had Rh^{-} and positive direct Coombs' test results (Rh incompatibility), those with jaundice in the first 24 hours of birth, and those underwent phototherapy before the first bilirubin measurement were excluded from the study.

This study was part of a large study which aimed to draw skin nomograms(16). The other purpose of this study was to determine maternal, childbirth, and neonatal factors related to neonatal skin bilirubin level and severe jaundice. The sample size was determined as 533 using G-power based on the relationship between at-risk groups and bilirubin discussed by Chawla et al. Since the design effect in cluster sampling is calculated twice the sample size, the final sample size was estimated at 1066 using G-power software (considering two-sided α= 0.05 and odds ratio= 0.7).

Sampling

After obtaining permission from the Ethics Committee of Tabriz University of Medical Sciences, Tabriz, Iran (IR.TBZMED.REC.1395.916), the researcher visited the teaching hospitals of Alzahra and Taleghani and identified all the eligible neonates through convenience sampling method, briefed their parents on the details of the study, and obtained their written informed consent. Data were collected using a researcher-made questionnaire based on the medical history of mothers and newborns as well as interviews with mothers.

Neonatal jaundice was measured using the Kj-8000 device on days 3-6 after birth, and the skin bilirubin level. Moreover, the need for phototherapy (severe jaundice) in neonates were determined based on American Academy of Pediatrics guidelines (AAP) for phototherapy. Neonates who were diagnosed with phototherapy based on TCB values and AAP phototherapy guidelines were referred to the relevant unit for further investigation and treatment in this study.

Data Collection Tools

A maternal, childbirth, and neonatal characteristics questionnaire and the Kj8000 device were utilized to collect data and determine the level of skin bilirubin, respectively. The maternal, childbirth, and neonatal characteristics questionnaire was designed in three sections after examining specialized texts. Section one included maternal characteristics, such as mother's age, level of education and occupation, spouse's level of education and occupation, family income sufficiency, place of residence, history of jaundice in previous children, history of stillbirth, mother's hypertension, preeclampsia and eclampsia, gestational diabetes, twin pregnancy, number of maternal ultrasound during pregnancy, and a history of bleeding in the first trimester.

Part two of this questionnaire seeks for information about neonatal characteristics, including infant's gender, gestational age at the time of birth, weight at the time of birth, blood type (i.e, four blood groups defined by the ABO blood group system include A, B, AB, and O), Rh, age of the first feeding, method of feeding, frequency of feeding, feeding the infant with water or sugar water during feeding intervals, meconium excretion after birth, and birth trauma.

Finally, part three included childbirth characteristics, such as the number of childbirths, current childbirth method, season of childbirth, induction with oxytocin during labor, epidural anesthesia during labor, type of anesthetic during labor, and rupture of membrane.

Content and face validity measures were used to assess the validity of this questionnaire. The questionnaires were given to 10 faculty members and corrections were applied based on their suggestions and opinions under the supervision of the supervisor.

The KJ-8000 device (Bilicheck) measures the severity of jaundice by detecting the level of bilirubin in the blood serum of neonates through the skin. No blood sample is required for using this device. Therefore, it imposes no pain, discomfort, or risk of bacterial infection on neonates. This device uses optical fibers and photoelectronic parts. The device shows the bilirubin level in terms of mg/dL or micromol/L on the monitor, as selected by the user. The probe must slightly touch the infant's forehead. This device directly measures the infant's blood serum bilirubin level and converts this level to numbers quickly and accurately.

To determine the reliability of the Bilicheck, five neonates were selected at the beginning of the sampling and two bilirubin measurements were performed on each neonate by two different individuals under the exact same conditions. Subsequently, the correlation between the two results was evaluated in each neonate.

In addition, the TCB was measured for 20 neonates who needed TSB to determine the reliability of the device before beginning the study. The TCB was checked for neonates diagnosed with jaundice and those who had blood tests (TSB) for confirmation in Taleghani Hospital, Tabriz, Iran, based on clinical examination by a neonatal physician. Subsequently, the results were compared and the reliability was confirmed with a correlation coefficient of 89%.

Data analysis

Data were analyzed in SPSS software (Version 24). Descriptive statistics, including mean, standard deviation, and percentage were utilized to describe each maternal, childbirth, and neonatal characteristic. To determine the relationship between each characteristic and skin bilirubin level, the adjusted and unadjusted generalized linear model was employed for controlling confounding variables. Moreover, the unadjusted and adjusted logistic regression with entering strategy was employed to control confounding variables and determine the relationship between each characteristic and severe jaundice.

Results

This cross-sectional study was conducted over ten months from January to October 2017. Of the 1066 neonates who entered the study, 555 (52%) were male and 511 (47.9%) were female. A total of 58.3% of neonates was given birth through cesarean section and the birth weight was 3000 to 3990 grams in 760 (71.3%) of the newborns. The mean age of mothers was 28.50 (6.16) years in this study. The neonates' available blood group was A in 37.6% and Rh^+ in 90% of the cases. The gestational age was between 35 and 36 weeks and six days in 43 (4%) neonates, between 37 and 39 weeks and six days in 715 (67.1%) cases, and more than 40 weeks in 308 (28.9%) newborns.

The most common blood group in the mothers was A^+ observed in 343 (32.8%) neonates, and the least common blood group was AB^- observed in 10 (0.9%) cases. The mean number of maternal ultrasound during pregnancy was 4.95 (2.06). About one-fifth of mothers (20.4%) had a history of jaundice in previous children. Only four newborns had birth trauma. The mean number of infant feeding per 24 hours was 16.1 (5.25). Water or sugar water was used during breastfeeding intervals for about 16% of the newborns (Table1).

Results of the unadjusted generalized linear model showed that bilirubin level correlated significantly with mother's occupation, history of jaundice in previous children, infant's age at meconium excretion, frequency of feeding, feeding the infant with water or sugar water during breastfeeding intervals, gestational age, method of childbirth, mother's blood type, season of childbirth, oxytocin induction during labor,

Table 1. Characteristics of healthy newborns with a gestational age of 35 weeks and over (n=1066)

Variables	Number (Percent)	Variables	Number (Percent)
Gender		Mother's age	28.50 (6.16)*
Male	555 (52)	Birth weight	
Female	511 (47.9)	2000-2990 g	250 (23.5)
Infant BG-RH		3000-3990 g	760 (71.3)
A+	60 (35.2)	4000 g and up	56 (5.3)
A-	4 (2.3)	Mother BG-RH	
B+	41 (24.1)	A+	343 (32.8)
B-	5 (2.9)	A-	50 (4.7)
AB+	11 (6.4)	B+	208 (19.9)
AB-	2 (1.1)	B-	26 (2.4)
O+	42 (24.7)	AB+	104 (9.9)
O-	5 (2.9)	AB-	10 (0.9)
Gestational age		O+	268 (25.7)
35-36 weeks and 6 days	43 (4)	O-	34 (3.2)
37-39 weeks and 6 days	715 (67.1)	Delivery method	
40 weeks and up	308 (28.9)	Vaginal	441 (41.3)
Number of maternal ultrasound during pregnancy	4.95 (2.06)*	Cesarean section	622 (58.3)
		Instrumental	3 (0.2)
Having a history of jaundice in previous children (Yes)	218 (20.4)	Number of feeding (per 24 hours)	16.1(5.25)*
Having trauma in birth (Yes)	4 (0.4)	Feeding the neonate with water or sugar water during breastfeeding intervals(Yes)	179 (16.7)

*Mean (Standard Deviation)

Table 2. The relationship between neonatal skin bilirubin level and maternal, childbirth, as well as neonatal characteristics based on an adjusted generalized linear model in healthy newborns with a gestational age of 35 weeks and over (n=1066)

Variable	Adjusted	
	B(95%CI*)	P-value
History of jaundice in previous children		
Yes	0	---
No	-0.93(-0.41 to -1.46)	0.003
Neonate's age at first meconium excretion	0.04 (0.07 to 0.01)	0.020
Frequency of feeding	-0.17 (-0.13 to -0.21)	<0.001
Gestational age		
35-36w,6d	0	---
37-39w,6d	0.91 (0.24 to -2.07)	0.194
40w and up	-2.49 (-1.27 to -3.71)	0.001
Mother's blood type		
A+	0	---
A-	0.45 (1.43 to -0.52)	0.445
B+	0.00 (0.61 to -0.59)	0.981
B-	-0.19 (1.12 to -1.52)	0.806
AB+	0.73 (1.50 to -0.02)	0.113
AB-	2.33 (4.76 to -0.09)	0.114
O+	0.29 (0.84 to -0.26)	0.389
O-	1.68 (2.90 to 0.46)	0.024
Number of maternal ultrasound during pregnancy	0.18 (0.29 to 0.07)	0.005

*95% Confidence Interval

diabetes in mothers, and frequency of ultrasound (P<0.05).

Moreover, results of the adjusted generalized linear model showed a significant association between skin bilirubin level and variables, such as a history of jaundice in previous children, infant's age at first meconium excretion, frequency of feeding, gestational age, mother's blood type, and number of ultrasounds (P<0.05, Table2).

Based on the results of unadjusted logistic regression, family income level, place of residence, history of jaundice in previous children, feeding the infant with water or sugar water during feeding intervals, infant's gestational age at birth, frequency of feeding the infant, season of childbirth, time of discharge, frequency of ultrasound during pregnancy, and mother's blood type and hypertension had a significant relationship with severe hyperbilirubinemia in neonates (P<0.05).

Furthermore, according to the results of adjusted logistic regression, a significant relationship was observed between severe jaundice and variables, including place of residence, history of jaundice in previous children, feeding the infant with water or sugar water in feeding intervals, frequency of feeding, gestational age, mother's blood type, time of discharge, and number of pregnancies (P<0.05, Table3).

Table3. The relationship between severe jaundice and maternal, childbirth, as well as neonatal characteristics based on adjusted logistic regression in healthy newborns with a gestational age of 35 weeks and over (n=1066)

Variable	Adjusted	
	OR (95%CI)*	P-value
Place of residence		
Personal	1	---
Rental	0.43 (0.72 to 0.26)	0.006
Mothers' parents' home	1	---
Spouse' parents' home	0.43 (1.11 to 0.17)	0.144
History of jaundice in previous children		
Yes	1	---
No	0.36 (0.61 to 0.21)	0.001
Feeding the neonate with water or sugar water in feeding intervals		
Yes	1	---
No	0.43 (0.71 to 0.26)	0.006
Frequency of feeding	0.91 (0.95 to 0.86)	0.002
Gestational age		
35-36w,6d	1	---
37-39w,6d	0.22 (0.49 to 0.10)	0.002
40w and up	0.12 (0.30 to 0.04)	<0.001
Mother’s blood type		
A+	1	---
A-	0.65 (2.47 to 0.17)	0.602
B+	1.31(0.45 to 0.75)	0.456
B-	3.28 (10.8 to 1.00)	0.100
AB+	1.67 (3.37 to 0.83)	0.226
AB-	1	---
O+	1.47 (2.55 to 0.84)	0.249
O-	4.93 (3.37 to 1.98)	0.004
Number of pregnancies		
1	1	---
2	0.65 (1.10 to 0.39)	0.183
3	0.66 (1.29 to 0.34)	0.315
4	0.10 (0.60 to 0.01)	0.035
5	0.43 (2.85 to 0.06)	0.469
6	1.03 (7.56 to 0.14)	0.977
Time of discharge		
Before 24 h	1	---
24-47.9 h	0.53 (0.93 to 0.30)	0.064
48-72 h	0.32 (0.78 to 0.13)	0.036

*Odds ratio (95% Confidence Interval)

Discussion

The present cross-sectional study aimed to examine various maternal, childbirth, and neonatal factors affecting the neonatal skin bilirubin level and severe jaundice in healthy neonates with the gestational age of ≥35 weeks and birth weight of ≥2000 g. Results revealed that infant’s skin bilirubin level correlated significantly with a history of jaundice in previous children, infant’s age at first meconium excretion, frequency of feeding, gestational age, mother’s blood type, and frequency of ultrasound. In addition, there was a significant relationship between severe jaundice and variables , including a history of jaundice in previous children, feeding the infant with water or sugar water during breastfeeding intervals, frequency of feeding the infant, gestational age, mother’s blood type, time of discharge from the hospital, place of residence, and number of pregnancies.

In this study, the history of jaundice in previous children was a factor related to jaundice. Saber et al. studied 170 newborns to identify predisposing factors for jaundice and measured the frequency of jaundice in the prenatal period. Results of their study showed a significant relationship between a history of jaundice in previous children with neonatal jaundice (13). The obtained result of the aforementioned study is consistent with that of the present study.

The infant’s weekly gestational age was another factor related to jaundice which was in line with the results reported by Saber et al. (13). Jaundice is the result of an imbalance between the production and removal of bilirubin. Neonates' liver is immature and their digestive system cannot excrete produced bilirubin. This causes unconjugated hyperbilirubinemia in preterm neonates (3).

Infant's age at meconium excretion is another factor related to neonatal bilirubin level. Studies by Bilgin et al. on 388 newborns showed no correlation between the method of feeding, method of childbirth, anesthesia, and type of anesthesia, infant gender, and time of meconium excretion with bilirubin levels 24-48 h after birth (11). In the present study, there was a significant relationship between the time of meconium excretion and bilirubin level which is inconsistent with the results of the above-mentioned study. Newborns who are fed in the first 3 h of birth usually excrete meconium in the following 4 hours. As 1 g of moist meconium contains 1 mg of bilirubin, delayed meconium excretion or its reduced frequency in neonates increases the intestinal-hepatic flow, thereby increasing neonatal jaundice (14).

Mother’s blood type was another factor related to jaundice in this study. Zahed Pasha et al. examined the relationship between the mother’s blood type and umbilical cord bilirubin level in 290 newborn term neonates. Results of their study indicated that mean umbilical cord bilirubin level was higher in neonates born of mothers with blood type O (17). In the present study, neonatal jaundice was higher in newborns of mothers with Rh-negative blood type O which is in line with the findings of the noted study. If mothers with blood type O have infants with blood type A or B, the risk of jaundice caused by blood incompatibility increases in neonates.

In the present study, the blood types of mothers were available, while the blood types of all neonates were not accessible and the relationship between the ABO blood group system and jaundice was not completely determined. Nevertheless, in mothers with blood type O, neonatal jaundice was significantly increased regardless of infants’ blood type.

In the present study, a significant relationship was observed between jaundice and feeding the infant with water or sugar water. In the study by Carvalho, the effect of feeding the infant with water was not significant on serum bilirubin level (18) which is inconsistent with the results of the present study. The consumption of sugar water may make the infant get used to feeding with the bottle and preferring it to breastfeed. The sugar water fed to the infant usually fills its small stomach leaving no room for the correct and adequate feeding with breast milk which causes jaundice as a result of inadequate breastfeeding.

The time of discharge from the hospital was another factor related to neonatal jaundice. Early discharge (less than 72 hours after birth) is increasing in healthy term neonates around the world. Since the highest serum bilirubin level is often observed three to five days after birth, an effective jaundice screening method can improve the immunity of early-discharged neonates. Delayed diagnosis of jaundice in newborns is one of the problems of early discharge (19).

In this study, neonatal jaundice was significantly decreased by increasing the frequency of breastfeeding. Dehydration and loss of received calories by the infant were other factors affecting the occurrence of jaundice. Adequate and periodic feeding is a factor preventing the occurrence of jaundice (20).

The Academy of Pediatrics (2004) recommends the identification of factors causing neonatal jaundice before discharge in order to prevent jaundice complications. It also suggests checking neonates on days 3-5 since the peak of serum bilirubin occurs at this time.

A strong point of this study was its large sample size, compared to similar studies. In addition, a non-invasive method was used for the measurement of neonatal jaundice in all steps of the study. One limitation of this study was its cross-sectional nature. The associations between neonatal jaundice and maternal, childbirth, and neonatal characteristics may not show an exact cause-effect relationship. Therefore, it is suggested that studies including cohort and case-control studies with a more powerful methodology. Another limitation of the present study was that in the studied hospitals, blood type, and Rh data were not sent for all neonates. Therefore, the infants’ blood type was known only when their mothers were Rh negative. Consequently, it was not possible for the researcher to assess blood type for all newborns. Therefore, the relationship between mothers’ and newborns’ blood type was not clearly delineated in this study.

Conclusion

The present study identified some maternal, neonatal, and childbirth factors related to neonatal jaundice, thereby raising the awareness of healthcare personnel for the identification of risk-factors of jaundice and prevention of its complications. Jaundice must be prevented as much as possible by educating parents on these risk-factors, increasing the frequency of breastfeeding, avoiding feeding with water and sugar water, and refraining from early discharge.

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Conflicts of interests

The authors declare no conflict of interest.

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