Original Article

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Umbilical Cord Bilirubin Level as a Predictive Indicator of Neonatal Jaundice

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ABSTRACT

BACKGROUND AND OBJECTIVE: Neonatal jaundice is a major problem among infants in the first weeks of life. Research on several indicators of severe neonatal jaundice including alpha-fetoprotein and umbilical cord bilirubin level has indicated contradictory results. Therefore, the aim of the present study was to evaluate the significance of umbilical cord bilirubin level as a predictive indicator of severe neonatal jaundice.

METHODS: This prospective, cross-sectional study was performed on 102 healthy infants, born to healthy mothers at Babol Clinic Hospital, Babol, Iran. After birth, 2 cc blood samples were obtained from the umbilical cord and the bilirubin level was measured in the hospital laboratory. The infants were followed-up after hospital discharge in terms of jaundice presentations. In case jaundice was diagnosed in infants, they were compared in treated and untreated groups.

FINDINGS: Clinical jaundice was not detected in 54 cases (52.94%). Overall, 48 neonates (47.05%) suffered from clinical jaundice and 10 cases (8.9%) presented with severe jaundice, requiring treatment based on the criteria proposed by the American Academy of Pediatrics (AAP). The mean umbilical cord bilirubin level was 1.82±0.42 mg/dl in the untreated group and 2.36±0.56 mg/dl in the treated group (P=0.000). The area under the ROC curve for umbilical cord bilirubin level was 0.722 in the treated group, based on the AAP criteria. The cut-off point of 2 mg/dl showed 80% sensitivity and 73% specificity in predicting severe jaundice (requiring treatment), based on the AAP criteria.

CONCLUSION: As the results indicated, measurement of umbilical cord bilirubin level and determination of a suitable cut-off point could be valuable in predicting severe jaundice in newborns.

KEY WORDS: Neonatal Jaundice, Umbilical Cord Blood, Bilirubin.

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Introduction

Neonatal jaundice is one of the major problems in newborns during the first weeks of life. This condition is a source of concern and anxiety for both parents and physicians. Early hospital discharge of newborns in the first week of life can be followed by severe hyperbilirubinemia in these

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infants. Moreover, early discharge without proper follow-up and parents' lack of knowledge on this issue can lead to severe neonatal jaundice (1,2). Jaundice is the most important problem during the neonatal period and failure to diagnose and treat hyperbilirubinemia can cause kernicterus and permanent disabilities (3,4). As the American Academy of Pediatrics (AAP) has recommended, at least two follow-up sessions should be set for infants, who are discharged within the first 48 hours after birth. The first session should be arranged between the first and third days after birth and the second session should take place between the third and fifth days after birth. If the follow-up of neonates is not possible, discharge should be postponed until the risk of jaundice is fully diminished (3-4 days after birth) (5). However, in some cases, the AAP criteria cannot be met due to high rates of bed occupancy at hospitals, families' unwillingness or limited follow-up facilities. Therefore, early detection of neonates at risk of severe jaundice is of great significance. In this regard, in a study by Rosenfeld in 1986, it was concluded that the risk of severe hyper bilirubinemia increases by 25% in infants with umbilical cord bilirubin level higher than 2 mg/dl (7). Considering the significance of diagnosing early jaundice and the need for prompt actions in order to prevent kernicterus, various methods have been applied to determine the associated risks. However, research on several markers such as alpha-fetoprotein and umbilical cord bilirubin level as early predictors of severe jaundice has indicated contradictory results. Therefore, in this study, we aimed to identify the significance of umbilical cord bilirubin level as a predictive indicator of neonatal jaundice.

Methods

This prospective, cross-sectional study was conducted on 102 healthy infants, born to healthy mothers during October-December 2013 at Babol Clinic Hospital, Babol, Iran. After birth, 2 cc blood samples were obtained from the umbilical cord and the bilirubin level was measured in the hospital laboratory. The bilirubin level was measured, using Autoanalyzer Sinnowa (DS301, China, 2013) at Babol Clinic Hospital. After discharge from the hospital, the infants were followed-up in terms of jaundice manifestations. Infants with clinical jaundice were referred to the hospital for the evaluation of serum bilirubin level, based on the physician's opinion.

If necessary, the infants received treatment according to the protocol proposed by Amir Kola Hospital, affiliated to Babol University of Medical Sciences (table 1). Full-term infants, born to healthy mothers, without any anomalies, preeclampsia, eclampsia or diabetes, with normal Apgar scores were included in the present study. The exclusion criteria were as follows: 1) hospitalization due to conditions other than jaundice, 2) occurrence of other diseases during the follow-up, and 3) lack of access to infants. Infants' demographic characteristics were recorded in a checklist.

The newborns were divided into two groups, based on their need for treatment: treated and untreated groups. For data analysis, t-test and Pearson's correlation coefficient test were performed, using SPSS version 22. The cut-off point was determined, using the operating characteristic curve (ROC) by determining the area under the curve.

Results

A total of 105 infants were evaluated in this study, among whom three newborns were excluded due to lack of access. As the results indicated, 54 subjects did not present with clinical jaundice (52.94%), whereas 48 cases (47.05%) suffered from clinical jaundice.

Table 1. The treatment protocol for neonatal jaundice at Amir kola Hospital (6)

Phototherapy		Phototherapy	Blood transfusion		Phototherapy termination
First day	Second day	Third day	With risk factors	Without risk factors	Age<3 days
5 mg/dl	10 mg/dl	15 mg/dl	20 mg/dl	25 mg/dl	10 mg/dl

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Also, 40 cases (39.21%) had a bilirubin level higher than or equal to 10 mg/dl. According to the findings, 20 patients (19.6%) were in need of for treatment, based on the hospital protocol. In all cases requiring treatment, phototherapy was the treatment of choice. Overall, 10 subjects (8.9%) were in need of for treatment, based on the AAP criteria. Based on the findings, 98 infants were delivered via cesarean section (96.1%), whereas 4 cases were born via vaginal delivery (3.9%). The mean gestational age of mothers was 38.7±0.6 weeks and their mean weight was 3644±4.6 g. The mean umbilical cord bilirubin level was 87.1 1.87 mg/dl, and the mean serum bilirubin level was measured to be 38.13 13.38 mg/dl (table 2).

As the results indicated, 54% of mothers had type O blood group, 25% had type B blood group, 18% had type A blood group and 3% had type AB blood group. There was no significant difference between the groups regarding umbilical cord bilirubin level. According to the treatment protocol of Amir Kola Hospital, the mean umbilical bilirubin level was 1.82±0.42 mg/dl in the untreated group and 2.11±0.54 mg/dl in the treated group (p=0.012) (table 3). The treatment criteria assigned by Amir Kola Hospital are below the standards, proposed by AAP. Therefore, we divided the infants, based on the AAP criteria. The infants were divided into two groups, based on these guidelines: requiring treatment and not requiring treatment. As the results indicated, the difference between the two groups was significant (P=0.000) (table 4). The area under the ROC curve of umbilical cord bilirubin level in treated subjects was 0.722, according to AAP criteria.

The cut-off point of 2 mg/dl showed 80% sensitivity and 73% specificity in predicting severe jaundice (indicative of need for treatment), based on the AAP protocol (CI=95%) (58-94) (fig 1, table 5).

Table 2. Mean values of maternal and neonatal variables

Variables	Number	Minimum	Maximum	Mean±SD
Maternal age (years)	102	17	40	28.56±4.55
Gestational age (weeks)	102	37.28	40.28	38.70±0.60
Weight (g)	101	2600	5000	3640.59±422.88
Umbilical cord bilirubin level (mg/dl)	102	1	3.23	1.87±0.46
Serum bilirubin level(mg/dl)	43	8.20	21	13.38±2.76

Table 3. Comparison of umbilical cord bilirubin level among untreated and treated infants, according to the treatment protocol of Amir Kola Hospital

Variables	Untreated group (mean±SD)	Treated group (mean±SD)	p-value
Maternal age (years)	28.43±4.43	29.10±4.95	0.56
Birth weight (g)	3644±424	3625±426	0.85
Gestational age (weeks)	38.7±0.61	38.54±0.52	0.18
Umbilical cord bilirubin level (mg/dl)	1.82±0.43	2.11±0.54	0.012
Number (%)	82(4.80)	20(6.19)	

Table 4. Comparison of different variables in treated and untreated groups, based on the AAP criteria

Variables	Untreated group (Mean±SD)	Treated group (Mean±SD)	p-value
Maternal age (years)	28.44±4.45	29.70±5.51	0.411
Birth weight (g)	3631±422	3720±441	0.534
Gestational age (weeks)	38.7±060	38.60±0.55	0.591
Umbilical cord bilirubin level (mg/dl)	1.82±0.42	2.36±0.56	0.000
Number (%)	92 (90)	10 (10)	

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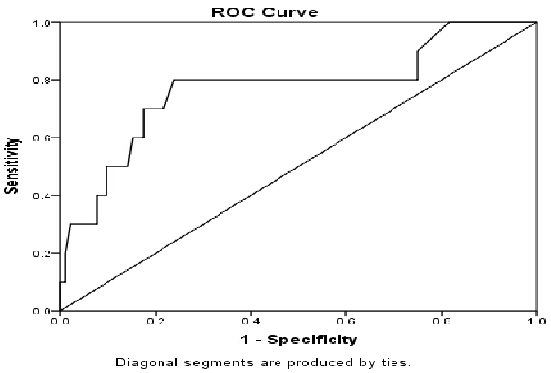

Figure 1. ROC curve of umbilical cord bilirubin level in the treated group, based on the AAP criteria (area under the curve=0.722)

Table 5. Sensitivity and specificity of different cut-off points

Cut-off points for umbilical cord bilirubin level (mg/dl)	Sensitivity	1-Specificity
1.9750	0.800	0.315
1.9900	0.800	0.293
2.0500	0.800	0.239
2.1100	0.700	0.217
2.1250	0.700	0.207
2.1650	0.700	0.196

Discussion

As the results of the present study indicated, umbilical cord bilirubin level of 2 mg/dl can be a suitable cut-off point for predicting neonatal jaundice, requiring treatment. In a study by Rosenfeld in 1986, umbilical cord bilirubin level was evaluated in a group of infants at risk of hyperbilirubinemia, undergoing phototherapy. As the results indicated, at an umbilical cord bilirubin level of>2 mg/dl, the risk of severe hyper bilirubinemia increased by 25% (7). Moreover, Bernaldo showed that almost 53% of infants require phototherapy in case the umbilical cord bilirubin level is higher than 2 mg/dl (8). In our study, there was a significant relationship between umbilical cord bilirubin level and severe jaundice, requiring phototherapy treatment, based on the AAP protocol. In the present study, the cut-off point of 2 mg/dl had a sensitivity of 80% and specificity of 73%. On the contrary, in a study by Jacobson et al., it was concluded that routine measurement of umbilical cord bilirubin level is neither necessary nor cost-effective (9).

However, in a study by Shahfarahat et al., in which umbilical cord bilirubin level was regarded as a predictor of pathological hyperbilirubinemia, bilirubin level was significantly different between the treated (bilirubin level >15 mg/dl) and untreated groups. In the mentioned study, the cut-off point of 2 mg/dl had a sensitivity of 68.86% and specificity of 61.18% (10). In our study, the assumed cut-off point showed 80% sensitivity and 73% specificity. Moreover, alpha-fetoprotein level has been evaluated as a predictive marker of neonatal jaundice. In this regard, Zahed Pasha and colleagues, who evaluated alpha-fetoprotein level for predicting severe neonatal hyperbilirubinemia, concluded that there was no significant relationship between alpha-fetoprotein level and severe jaundice (10, 11). On the other hand, in a study by Tan et al., umbilical cord alpha-fetoprotein level was confirmed as a screening test for neonatal jaundice (12). Contrarily, in another study, Zahed Pasha et al. found no significant difference in the level of umbilical cord bilirubin level between infants with different blood groups (13). Similarly, in our study, no statistically significant difference was observed in the level of umbilical cord bilirubin level between various blood groups. In some studies, umbilical cord bilirubin level was shown to have good sensitivity and specificity, with a high negative predictive value (NPV) (14-16).

Table 6. Comparison between the present findings and previous research (14-16)

Conducted Research	The cut-off point of umbilical cord bilirubin level	Sensitivity (%)	Specificity (%)	NPV (%)
The present study	2	80	73	96.6
Zakia Nahar, 2009 (14)	2.5	77	98.6	96
AlaaEldin A, 2013 (15)	2.15	50	97	97.1
Venkatamurthy M, 2014 (16)	2.1	100	61.04	100

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In Iran, due to high rates of bed occupancy at hospitals, infants are discharged much earlier (within less than 24 hours after birth) than the early discharge recommended time (48 hours after birth). Moreover, high rates of hospital readmission for jaundice have been reported and lack of a precise predictive test for severe hyperbilirubinemia is strongly felt. Based on the findings of the present study (presented in the table above), umbilical cord bilirubin level lower than 2 mg/dl shows that the infant may be discharged early. In conclusion, determination of umbilical cord bilirubin level for predicting severe neonatal hyperbilirubinemia is quite valuable. However, this indicator has not yet become a practical routine test at hospitals; therefore, further research in this area is highly recommended.

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References

1.Facchini FP, Mezzacappa MA, Rosa IR, MezzacappaFilho F, Aranha-Netto A, Marba ST. Follow-up of neonatal jaundice in term and late premature newborns. J Pediatr (Rio J). 2007;83(4):313-22.

2.Chou HC, Chien CT, Tsao PN, Hsieh WS, Chen CY, Chang MH. Prediction of severe neonatal hyperbilirubinemia using cord blood hydrogen peroxide: A prospective study. PLoS One. 2014;9(1):e86797.

3.Sgro M, Campbell D, Shah V. Incidence and cause of sever hyperbilirubinemiain Canada. CMAJ. 2006;175(6):587-90.

4.Egube BA, Ofili AN, Isara AR, Onakewhor JU. Neonatal jaundice and its management: Knowledge, attitude, and practice among expectant mothers attending antenatal clinic at University of Benin Teaching Hospital, Benin City, Nigeria. Niger J Clin Pract 2013;16:188-94.

5.American Academy of Pediatrics Subcommittee on Hyperbilirubinemia. Management of hyperbilirubinemia in the newborn infant 35 or more weeks of gestation. Pediatrics 2004;114(1):297-316.

6.Ahmadpour M, Zahedpash Y, Taghavi M, Bijani A. Effects of phototherapy on platelet count, reticulocyte count and White Blood Cells in Term Neonate with Hyperbilirubinemia. Med J Mashhad Univ Med Sci. 2013;55(4):211-7.[In Persian]

7.Rosenfeld J. Umbilical cord bilirubin levels as a predictor of subsequent hyperbilirubinemia. J Fam Pract. 1986; 23(6):556-8.

8.Bernaldo AJ, Segre CA. Bilirubin dosage in cord blood: could it predict neonatal hyperbilirubinemia? Sao Paulo Med J. 2004;122(3):99-103.

9.Jacobson MP, Bernstein HH. Limited diagnostic value of routine cord blood bilirubin determinations. Clin Pediatr. 1982;21(10):610-2.

10.Farhat A, Alizadeh Ghamsari A, Mohamadzadeh A, Khodadadi A, Rezaei M. Does umbilical cord bilirubin level have predictive value in pathologic neonatal hyperbilirubinemia?. Iran J Neonatol. 20013;4(1):32-5.

11.Zahedpasha Y, Ahmadpour-Kacho M, Khalafi J. Cord blood α-fetoprotein as a predictive index for indirect hyperbilirubinemia in term neonates. Caspian J Intern Med. 2011;2(4):326-30.

12.Tan KL, Loganath A, Roy AC, Goh HH, Karim SM, Ratnam SS. Cord plasma alpha-fetoprotein values and neonatal jaundice. Pediatrics. 1984;74(6):1065-8.

13.Zahedpasha Y, Hajian K, Azadafrooz S, Baleghi M. Relationship between the cord blood bilirubin level and maternal blood group. J Babol Univ Med Sci. 2007;9(5):32-6. [In Persian]

14.Nahar Z, Abdulmannan S, Kumar Dey S, Mitra U, Selimuzzamann SM. The value of umbilical cord blood bilirubin measurement in predicting the development of significant hyperbilirubinemia in healthy newborn Bangladesh J Child Health. 2009;33(2):50-4.

15.Zeitouna AA, Elhagrasya HF, Abdelsatar DM. Predictive value of umbilical cord blood bilirubin in neonatal hyperbilirubinemia. Egypt Pediatr Associat Gazet. 2013;61(1):23-30.

16.Venkatamurthy M, Murali SM, Mamatha S. A comparison study: cord serum albumin is compared with cord serum bilirubin as a risk indicator in predicting neonatal jaundice. J Evolu Med Dent Sci. 2014;3(15):4017-22.

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