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Original Article

The Role of Cord Blood Gas Parameters in Prediction of Significant Hyperbilirubinemia among Healthy Term Newborns

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ABSTRACT

Objective: Hyperbilirubinemia is one of the most common problems of late preterm and term babies. The aim of our study was to evaluate the relation between cord blood bilirubin levels. blood gas parameters. and the development of significant hyperbilirubinemia.

Methods: Our study included 812 babies who met the inclusion criteria. Umbilical cord blood bilirubin levels and blood gas analysis were determined. Transcutaneous bilirubin (TcB) values were recorded at postnatal 0, 12, 24, and 48 h. Babies with TcB levels above the 75% percentile were classified as severe hyperbilirubinemia; babies whose bilirubin level was below the 75% percentile were included in the control group. Demographic data were obtained from the birth records of babies.

Results: The average birth weight and gestational age were 3265.99±482.14 g and 38.57±1.44 weeks. respectively. The mean pH, pCO_2, HCO_3, BE, and lactate levels were 7.28±0.06, 49.26±8.04, 22.45±2.46, −3.99±2.45, and 2.98±1.08, respectively. The mean cord bilirubin measurements were found to be 1.99±0.66 mg/dl. TcB levels at 0, 12, 24, and 48 h were found to be 1.92±0.85, 3.75±1.26, 6.01±1.91, and 8.63±2.36 mg/dl, respectively. We found a statistically significant correlation between PN 0 h TcB measurements and cord blood bilirubin levels. While cord blood bilirubin and PN 0 h TcB measurements were found to be highly correlated (r=0.638; p<0.01), cord blood bilirubin and 12, 24, and 48 h TcB measurements were moderately correlated (r=0.573; p<0.01), (r=0.559; p<0.01) (r=0.482; p<0.01). There was not any statistically significant difference regarding cord blood pH, PCO_2, HCO_3, and lactate levels between groups with or without significant hyperbilirubinemia (p>0.05). Only cord blood base access levels were found to be significantly higher in group with significant hyperbilirubinemia (p=0.001).

Conclusion: We found a statistically significant correlation between PN 0 h TcB measurements and cord blood bilirubin levels. Postnatal 0 h TcB measurements may be used to screen significant hyperbilirubinemia. We also found a significant relation between cord blood base access levels and development of significant hyperbilirubinemia. Cord blood base access levels may help to screen significant hyperbilirubinemia.

INTRODUCTION

Hyperbilirubinemia is one of the most common problems of late preterm and term babies. Hyperbilirubinemia is observed in 60% of newborn babies in the 1st postnatal week. Decreased hepatic conjugation and secretion of bilirubin and increased destruction of fetal erythrocytes may lead to the development of significant hyperbilirubinemia.[1,2]

Acute bilirubin encephalopathy may result in neurological, auditory, and motor damage in infants with underlying disease and other perinatal risk factors. Nowadays, due to the policy of early discharge, follow-up in terms of hyperbilirubinemia becomes difficult.[3] To reduce the risk of neurological involvement due to hyperbilirubinemia, it is recommended that every newborn's bilirubin level should be evaluated before discharge.[4,5]

As a result of the oxidative stress exposure after birth, due to the destruction of the erythrocytes, the metabolic degradation of "heme" increases.[6] In addition to this physiological mechanisms, it has been shown that hypoxia, perinatal asphyxia, and acidosis are risk factors for the development of significant hyperbilirubinemia.[7,8] The pH and base deficit values in the cord blood gas analysis were shown to reflect the hypoxic effect experienced in the perinatal period in newborns.

The aim of our study was to identify babies with significant hyperbilirubinemia development risk using cord blood gas values and contribute to the reduction of morbidity associated with hyperbilirubinemia.

MATERIALS AND METHODS

This prospective study included 812 babies who met the inclusion criteria and were born in our hospital.

Babies with congenital anomalies, severe intrauterine growth retardation, direct Coombs (+) Rh and ABO incompatibility, and babies who needed to be hospitalized in the neonatal intensive care unit for any reason and whose family did not give consent to participate in the study were not included in the study. Ethics committee approval was obtained from the local Clinical Research Ethics Committee. The families of the babies included in the study were informed in detail about the study and informed consent was signed. Demographic data of the babies were recorded.

Sample collection

Umbilical cord blood samples were collected in the delivery room. Capillary cord blood gas and total bilirubin levels were measured. TcB were measured over forehead within 10 min after blood collection. Follow-up during nursery care, TcB levels were measured and recorded for babies born with normal delivery and for those with C/S mode of delivery at the postnatal 0–12–24 h and postnatal 0–12–24 and 48 h, respectively.

The babies whose TcB values were at or above the 75 percentile in any measurement according to the Bhutani nomogram constituted the study group, and the group whose bilirubin values were below 75 percentile constituted the control group.

Statistical analysis

Number Cruncher Statistical System program was used for statistical analysis. Descriptive statistical methods (mean, standard deviation, median, frequency, percentage, minimum, and maximum) were used while evaluating the study data. The suitability of quantitative data to normal distribution was tested by Shapiro–Wilk test and graphical analysis. Student's t-test was used for comparing normally distributed quantitative variables between two groups. In multivariate analysis, independent predictors in predicting outcome using probable factors were examined by logistic regression analysis. Statistical significance was accepted as $p<0.05$.

RESULTS

Eight hundred and twelve babies were included in the study. The demographic characteristics of the cases are shown in Table 1. In terms of demographic characteristics, there were no difference between the groups ($p>0.05$). It was observed that 410 (50.5%) babies had significant hyperbilirubinemia in the first postnatal 48 h.

Table 1. Demographic characteristics of groups

	Mean±SD
Gestational week, weeks	38.57±1.44
Gender, n (%)	
Female	404 (49.7)
Male	408 (50.3)
Birth weight (gr ±SD)	3265.99±482.14
Route of delivery, n (%)	
NSVD	426 (52.5)
C/S	386 (47.5)
Nationality, n (%)	
TC	572 (70.5)
Others	240 (29.5)

NSVD: Normal spontan vaginal delivery; SD: Standard deviation; TC: Turkish Republic.

Table 2. Umbilical cord bilirubin and TcB values of the groups

	Min-Max. (Median)	Mean±SD
Cord bilirubin (mg/dl)	0.7–3.93 (1.9)	1.99±0.66
Transcutan bilirubin (mg/dl)		
0. hour (n=288)	0.4–4.0 (1.9)	1.92±0.85
12. hours (n=293)	1.2–10.5 (3.5)	3.75±1.26
24. hours (n=297)	1.4–13.6 (5.9)	6.01±1.91
48. hours (n=279)	1.2–15.3 (8.4)	8.63±2.36

TcB: Transcutaneous bilirubin; SD: Standard deviation.

Babies' umbilical cord bilirubin values ranged from 0.7 to 3.93 mg/dl, and the average cord bilirubin value was found to be 1.99±0.66 mg/dl. TcB values were 1.92±0.85 mg/dl, 3.75±1.26 mg/dl, 6.01±1.91 mg/dl, and 8.63±2.36 mg/dl at postnatal 0, 12, 24, and 48 h, respectively. The median and mean values of cord and TcB values are shown in Table 2. Statistically significant correlation was found between

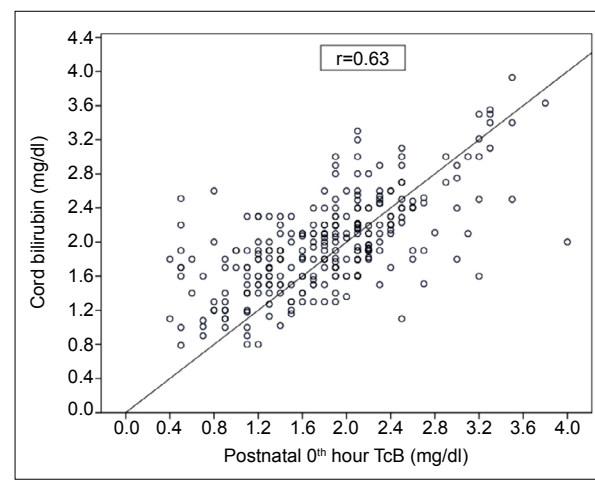

Figure 1. Correlation between cord bilirubin and postnatal 0th hour TcB values.

umbilical cord and transcutaneous postnatal 0 h bilirubin values (p<0.01; r=0.63) (Fig. 1).

A moderate correlation was found between cord bilirubin and TcB at the 12, 24, and 48 h, respectively ([r=0.573; p<0.01], [r=0.559; p<0.01], and [r=0.482; p<0.01]).

Table 3. Apgar and blood gas parameters of groups

	Min-Max. (Median)	Mean±SD
APGAR 1st	7–9 (8)	8.15±0.59
APGAR 5th	7–10 (9)	8.80±0.48
pH	7.26–7.45 (7.29)	7.28±0.06
PCO_2	25.5–78 (48.9)	49.26±8.04
HCO_3	18.7–33 (22.3)	22.45±2.46
BE	-8.2–4.1 (-4.0)	-3.99±2.45
Lactat	0.9–7.9 (2.7)	2.91±1.08

SD: Standard deviation.

Table 4. Comparison of blood gas parameters of groups

	Severe Hyperbilirubinemia		p
	(+) (n=410)	(-) (n=402)	
pH			
Min-Max, (Median)	7.2–7.5 (7.3)	7.2–7.4 (7.3)	[a]0.246
Mean±SD	7.28±0.06	7.29±0.06	
PCO_2 (mmHg)			
Min-Max, (Median)	30.8-75.3 (49.8)	25.5–78 (48)	[a]0.333
Mean±SD	49.72±8.39	48.83±7.7	
HCO_3 (mmol/L)			
Min-Max, (Median)	17.2–33 (22.2)	15.7–31.8 (22.3)	[a]0.09
Mean±SD	22.27±2.35	22.61±2.48	
BE (mmol/L)			
Min-Max, (Median)	-8.9–4.1 (-4.4)	-7.8–4.1 (-3.7)	[a]0.001
Mean±SD	-4.31±2.42	-3.69±2.44	
Lactat (mmol/L)			
Min-Max, (Median)	1.1–7.9 (2.7)	0.9–6.4 (2.7)	[a]0.997
Mean±SD	2.99±1.22	2.84±0.92	

[a]Student-t Test. SD: Standard deviation.

Umbilical cord blood gas pH and PCO_2 measurements were 7.28±0.06 and 49.26±8.04 mmol/l, respectively; HCO_3, BE, and lactate measurements were found as 22.45±2.46, −3.99±2.45, and 2.91±1.108, respectively.

The median and mean values for the Apgar and blood gas parameters of the whole group are shown in Table 3.

Between two groups while pH, PCO_2, HCO_3, and lactate values did not show a statistically significant difference (p>0.05), the base deficit measurements were found to be significantly higher in the group with significant hyperbilirubinemia (p=0.001) (Table 4).

Regarding the effect of blood gas parameters, cord bilirubin, and postnatal 0th h transcutaneous bilirubin (TcB) values on the development of hyperbilirubinemia, the base deficit value was found to have a statistically significant predictive effect (Table 5).

Umbilical cord bilirubin and postnatal 0th h TcB values were found to have a predictive effect on the development of hyperbilirubinemia.

DISCUSSION

In our study, it was found that the umbilical cord blood base deficit value is associated with the development of severe hyperbilirubinemia and may be used to predict the risk of developing hyperbilirubinemia. A high degree of correlation (r=0.638; p<0.01) was shown between postnatal 0 h TcB and cord bilirubin, while a moderate correlation was found between cord bilirubin and 12, 24, and 48 h TcB ([r=0.573; p<0.01], [r=0.559; p<0.01], and [r=0.482; p<0.01]).

Various studies have shown that erythrocytes not only serve as oxygen transporter but also exhibit oxygen-sensitive responses and their behavior is regulated autonomously depending on oxygen level.[9] Hypoxic events cause hemolysis of erythrocytes and "heme" degradation products are formed after exposure to hypoxia.[10,11] In newborns exposed to hypoxia, the risk of developing hemolysis and hyperbilirubinemia increases as a result of these physiological mechanisms. Neurons exposed to hyperbilirubinemia and hypoxic insults, tend to experience two different types of cell damage – necrosis and apoptosis – and this may result as more severe neuron damage.[12,13]

Table 5. Multiple logistic regression results for factors affecting the development of significant hyperbilirubinemia

Risk factors	B	SE	RR (95% CI)		Exp(B)	p
			Min	Max.		
pH	.119	2.855	.003	1.072	.880	0.985
HCO_3 (mmol/L)	.121	.109	.912	1.396	.998	0.267
BE (mmol/L)	-.088	.038	.957	1.268	1.081	0.02
Lactat (mmol/L)	-.078	.155	.898	1.465	.980	0.117
Cord bilirubin (mg/dl)	1.075	.345	1.489	5.764	2.929	0.002
Bilirubin levels at postnatal 0th hour (mg/dl)	.968	.269	1.554	4.455	2.631	<0.001

RR: Relative Risk; CI: Confidence Interval; Tcb: Transcutan bilirubin.

In addition to these, by negatively affecting the binding of albumin and bilirubin, hypoxia and acidosis may accentuate the brain damage due to hyperbilirubinemia.[14]

The pH and base deficit values in the cord blood gas were shown to reflect the hypoxic effect experienced in the perinatal period in newborns. Studies have also reported that the umbilical cord blood gas base deficit value may reflect the duration of hypoxia[3] and the base deficit is a good indicator in predicting the severity of metabolic acidosis.[15] Zanardo et al.[16] measured cord blood gas and bilirubin levels at postnatal 36 h and reported that HCO3, lactate, and base deficit values were statistically significantly higher in the cord blood gas of babies who developed severe hyperbilirubinemia. In our study, cord blood gas BE values of babies who developed severe hyperbilirubinemia were found to be significantly higher and base deficit levels were shown to have a significant predictive effect on the development of severe hyperbilirubinemia. According to these results, the cord base deficit value can be considered as a valuable parameter in predicting hyperbilirubinemia. In our study, we could not find any statistically significant difference regarding cord blood pH, PCO_2, HCO_3, and lactate levels between two groups ($p>0.05$).

Protecting babies from the adverse effects of severe hyperbilirubinemia seems possible by timely recognition of high-risk babies and appropriate follow-up.[17] The Turkish Neonatal Society also recommends measuring the bilirubin level of each newborn before discharge, to determine the risk group and perform appropriate follow-up.[18,19]

There are many studies showing that TcB measurements can be used in predicting and monitoring the risk of hyperbilirubinemia. TcB levels are found to be highly correlated with serum bilirubin values in preterm and term babies[20,21] and reduce the need for blood sampling.[22] It is recommended that all babies should be screened routinely with transcutaneous bilirubinometry before discharge. There are many studies evaluating the correlation between transcutaneous and serum bilirubin values. The correlation coefficient (r) between TSB and TcB measurements was reported as 0.91 and 0.89 by Keren et al.[23] and Szabo et al.,[24] respectively. In the study of Rubaltelli et al.,[25] it was shown that there is a high correlation (r=0.89) between TSB and TcB. To evaluate babies with TcB levels before discharge. TcB percentile curves were created for postnatal 1st week of life, but these curves can be used especially after the postnatal 12 h. Although there have been studies investigating the correlation between TcB and TSB at postnatal 6 h and after, there is not any study reporting the relationship between cord blood bilirubin values and 0 h TcB measurements. In our study, there was a high-level correlation between postnatal cord bilirubin and 0 h TcB levels ($r=0.638$; $p<0.01$); and a moderate correlation was found between the 12, 24, and 48 h TcB levels ($r=0.573$; $p<0.01$), ($r=0.559$; $p<0.01$), and ($r=0.482$; $p<0.01$). Although there are not enough data in the literature about this topic, our results suggest that 0 h TcB measurements may be useful in predicting severe hyperbilirubinemia.

Umbilical cord bilirubin measurement is a simple, reliable, and inexpensive method that can be used to identify high-risk babies in the neonatal period. Many studies have shown that cord bilirubin is valuable in predicting severe hyperbilirubinemia.[26–29] It has been reported that the cord bilirubin value may be useful in predicting hyperbilirubinemia, but it may give more precise results if used concomitantly with other risk markers.[26] In our study, we found that cord bilirubin values were significantly higher in the group with severe hyperbilirubinemia compared to the other group.

The strength of our study is that bilirubin was monitored with frequent measurements in the first 2 days starting from the postnatal 0 h. The limitations of our study are; the study was conducted in a single center with a limited number of babies and TSB could not be measured simultaneously with TcB measurements.

CONCLUSION

As a result; in our study, a significant relationship was found between the cord blood base deficit and the development of severe hyperbilirubinemia. Cord blood base deficit value, along with serial TcB measurements, may be used to differentiate high-risk babies for developing severe hyperbilirubinemia. Postnatal 0 h TcB measurement, which shows a high correlation with cord bilirubin measurements, may be a valuable parameter in predicting the risk of developing severe hyperbilirubinemia.

Ethics Committee Approval

This study approved by the İstanbul Training and Research Hospital Clinical Research Ethics Committee (Date: 21.08.2020, Decision No: 2498).

Informed Consent

Prospective study.

Peer-review

Externally peer-reviewed.

Authorship Contributions

Concept: E.G., D.A.; Design: E.G, D.A., S.C.; Supervision: D.A, S.C.; Materials: E.G., N.K.; Data: E.G., N.K., G.A.; Analysis: D.A.; Literature search: E.G., N.K.; Writing: E.G, D.A., N.K.; Critical revision: E.G., D.A., S.C.

Conflict of Interest

None declared.

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Sağlıklı Term Bebeklerde Kord Kan Gazı Parametrelerinin Ciddi Hiperbilirubinemiyi Ön Görmedeki Yeri

Amaç: Hiperbilirubinemi geç preterm ve term bebeklerin en önemli sorunlarından biridir. Çalışmamızda kordon kanı bilirübin değerleri, kordon kan gazı asidoz belirteçleri ile tedavi gerektiren hiperbilirubinemi arasındaki ilişkiyi değerlendirmeyi amaçladık.

Gereç ve Yöntem: Çalışmamıza 812 bebek dahil edildi. Göbek kordonu kan örneğinde bilirubin ve kan gazı parametreleri çalışıldı. Bebeklerin postnatal 0., 12., 24 ve 48. saatlerde transkutan (TcB) bilirubin düzeyleri ölçüldü. Transkutan bilirubin değeri 75% persantil üzerindekiler çalışma grubuna; altındakiler ise kontrol grubuna dahil edildi. Bebeklerin demografik doğum kayıtlarından elde edildi.

Bulgular: Bebeklerin ortalama gestasyon haftaları 38.57±1.44 hafta, doğum tartıları ise 3265.99±482.14 gramdı. Bebeklerin ortalama pH, PCO_2, HCO_3, BE ve laktat ölçümleri sırasıyla 7.28±0.06, 49.26±8.04 mmHg, 22.45±2.46 mmol/L, −3.99±2.45 mmol/L ve 2.91±1.108 mmol/L olarak saptandı. Ortalama kordon bilirubin değeri 1.99±0.66 mg/dl idi. Postnatal 0., 12., 24. ve 48. saat transkutan bilirubin ölçümleri sırasıyla 1.92±0.85, 3.75±1.26, 6.01±1.91 ve 8.63±2.36 mg/dl olarak saptandı. PN 0. saat TcB ile kordon bilirübini arasında istatistiksel anlamlı bir ilişki bulunmuştur. Kordon bilirübin değeri ile 0. saat TcB arasında yüksek korelasyon (r=0.638; p<0.01), kordon bilirübin ile 12., 24. ve 48. saat TcB arasında ise orta düzeyde korelasyon bulundu (r=0.573; p<0.01), (r=0.559; p<0.01) ve (r=0.482; p<0.01). Ciddi hiperbilirubinemi gelişen ve gelişmeyen bebeklerin pH, PCO_2, HCO_3 ve laktat ölçümleri, istatistiksel olarak anlamlı farklılık göstermemekte iken (p>0.05), baz açığı ölçümleri hiperbilirubinemi gelişen grupta anlamlı düzeyde yüksek bulundu (p=0.001).

Sonuç: Çalışmamızda 0. saat TcB ölçümü ile kord bilirübin ölçümleri arasında korelasyon olduğunu saptadık. Postnatal 0.saat TcB ölçümü ciddi hiperbilirübinemi gelişimini öngörmede kullanılabilir.Kan gazı baz açığı düzeyi ile ciddi hiperbilirubinemi gelişimi arasında da anlamlı bir ilişki saptadık. Kordon kanı baz açığı değeri hiperbilirübinemiyi öngörmede önemli olabilir.

Anahtar Sözcükler: Asidoz; baz açığı; hiperbilirubinemi; kordon kanı bilirubini; kordon kan gazı.