Original Article

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Association of Cord Blood Bilirubin with Neonatal Hyperbilirubinemia: A Hospital Based Study

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Abstract

Background: Around 60% of term newborns have jaundice within the first week of life. Increased bilirubin synthesis (due to red blood cell breakdown), incorrect uptake, and decreased clearance by the young liver induce this physiological change. Jaundice is a typical condition among infants. Neonatal hyperbilirubinemia (NH) can induce kernicterus in otherwise healthy newborns. **Subjects and Methods:** After meeting the eligibility criteria, a minimum of 74 healthy full-term babies were enrolled. All full term neonates (Gestation age 37 weeks to 42 weeks) are included in our study, regardless of mode of delivery, and newborns with risk factors for severe hyperbilirubinemia, such as jaundice observed within the first 24 hours, ABO and/or Rh incompatibility, cephalohematoma or significant bruising, significant co morbidities requiring N.I.C.U. admission, are excluded. **Results:** This cross-sectionall study included 74 healthy term newborns who were monitored during the first five days after birth. The findings of the investigation were analysed utilising statistical methods. **Conclusion:** Significant hyperbilirubinemia affects 5.4 percent of the people in our sample. TSB 15 mg/ dl at 48 hours of life is considered significant jaundice.

Keywords: Hyperbilirubinemia, Newborns and Cord Bilirubin.

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Introduction

During the first week of life, around 60% of term infants develop jaundice.[1,2] It occurs as a result of a physiological shift caused by increased bilirubin synthesis (due to red blood cell disintegration), improper uptake, and impaired clearance by the immature liver. Jaundice in newborns is a common occurrence. In otherwise healthy neonates, neonatal hyperbilirubinemia (NH) can cause kernicterus. This can be easily avoided if excessive hyperbilirubinemia for age is diagnosed and treated promptly.[2] Newborns can be screened for bilirubinemia severity before being discharged from the hospital, which may aid in the early detection of newborns who are at risk for excessive hyperbilirubinemia during the first week of life.[3] It's impossible to tell which of these babies may develop substantial hyperbilirubinemia (Total Serum Bilirubin 15 mg/dl). Approximately 3% of normal term newborns have significant hyperbilirubinemia.[4] The incidence of hyperbilirubinemia varies depending on various techniques of bilirubin quantification in different laboratories, the frequency of breast feeding, ethnic makeup of persons, and regional variations.[5] Some healthy full-term neonates who were released early with no evident hemolysis had severe jaundice and kernicterus.[6] The American Academy of Pediatrics (AAP) recommends that neonates who are discharged within 48 hours have a follow-up visit within 2-3 days to detect substantial jaundice and other issues.[7] Due to limited follow-up facilities in poor nations like India, this proposal is not feasible. When compared to the treatment of severe neonatal jaundice with exchange transfusion, which is time consuming, costly, linked with complications, and needs specialised people, early treatment of jaundice with phototherapy is effective, straightforward, and inexpensive. As a result, early detection of jaundice is an appealing method for identifying babies at risk of NH. Many researchers have looked for a simple marker to predict hyperbilirubinemia and its course in infants, such as cord bilirubin estimate, bilirubin estimation between 6 and 24 hours of age, predischarge hour specific bilirubin estimation,[8] and transcutaneous bilirubin measurement. Cord Bilirubin levels

are simple to measure and may serve as a useful predictor of future hyberbilirubinemic events. With this in mind, the current study aims to assess the capacity of cord bilirubin levels to predict later hyperbilirubinemia in healthy term babies.

Subjects and Methods

This current Study was conducted in Department of Pediatrics, World College of Medical Sciences Research and Hospital, Jhajjar Haryana, India from March, 2018 to September, 2019. After meeting the eligibility criteria, a minimum of 74 healthy full-term babies were enrolled. All full term neonates (Gestation age 37 weeks to 42 weeks) are included in our study, regardless of mode of delivery, and newborns with risk factors for severe hyperbilirubinemia, such as jaundice observed within the first 24 hours, ABO and/or Rh incompatibility, cephalohematoma or significant bruising, significant co morbidities requiring N.I.C.U. admission, are excluded. Parents or guardians provide written informed consent. A detailed obstetric and medical history of the mother is gathered, and the New Ballard Score is used to confirm the gestational age of each newborn. A sample of cord blood is taken and utilised for the following tests: haemoglobin and hematocrit, blood group and Rh factor, and serum bilirubin (Total, Direct & Indirect). For the purposes of this study, "Cord Blood Hyperbilirubinemia" is defined as a total bilirubin level in the cord blood of less than 3 mg/dl.[9] The newborns' venous blood samples are taken 48 hours and five days after delivery. On these samples, the following tests are performed: haemoglobin and hematocrit, serum bilirubin- (Total, Direct & Indirect). If necessary, serum bilirubin levels are checked more often. The blood sample was kept out of the light. The material was kept chilled between 2 and 8 degrees Celsius until serum bilirubin was determined. The diazotized sulfanilic test was used to estimate serum bilirubin within 12 hours of sample collection. This bilirubin measurement method is based on the principle that bilirubin combines with diazotized sulphanilic acid in an acidic solution to create pink azobilirubin, with absorbance proportional to bilirubin concentration. Because direct bilirubin is water soluble, it reacts immediately in an acidic environment. Indirect or unconjugated bilirubin, on the other hand, is solubilized with a surfactant before reacting similarly to direct bilirubin. Additional investigations are carried out in accordance with the circumstances. SPSS-16 statistical software is used to analyse the findings of the research.

Results

The study yielded the following outcomes. This cross-sectionall study included 74 healthy term newborns who were monitored during the first five days after birth. The findings of the investigation were analysed utilising statistical methods. Significant hyperbilirubinemia affects 5.4 percent of the people in our sample. TSB 15 mg/ dl at 48 hours of life is considered significant jaundice [Table 1].

Table 1: hows the study population and the severity of jaundice.

	Significant Jaundice
Total	Number (%)
74	4

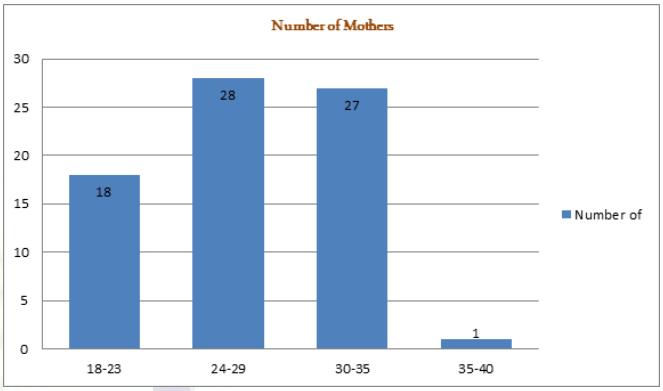

Figure 1: Shows the number of mothers participated a/c to age group.

[Figure 1] Shows the Parity.

Table 2: Maternal Details (N = 74)

Mothers details		Number of Mothers (%)
Mother age	18-23	18(24.5%)
	24-29	28(37.8%)
	30-35	27(36.5%)
	35-40	01(1.35%)
Parity	Primi	38(51.4%)
	Multi	36(48.4%)
Blood group	A+	20(27.02%)
	B+	23(31.08%)
	O+	22(29.7%)
	AB+	09(12.2%)

Discussion

Hyperbilirubinemia is a typical issue in most newborns. Jaundice is observed in around 60% of term infants and 80% of preterm infants within the first week of life. In normal

Table 3: Details of Neonates Studied (N=74)

Details of Neonates		Number of Neonates
Gender	Male	39(52.7%)
	Female	35(47.3%)
Weeks of Gestation	37-38	56(75.7%)
	39-40	18(24.3%)
Birth weight(kg)	2.50-3.00	59(79.7%)
	3.01-3.50	14(18.9%)
	3.51-4.00	01(1.35%)
Blood group	A+	18(24.3%)
	B+	23(31.1%)
	O+	21(28.4%)
	AB+	12(16.2%)

Table 4: Effect of Oxytocin Induction on Jaundice.

		Number of Neonates
Oxytocin Induced	Yes	33(54.6%)
	No	41(55.4%)
Total		74(100.0%)

Table 5: History of neonatal jaundice in previous siblings.

H/O Neonatal Jaundice	Number of neonates (%)
Yes	1 (2.9%)
No	34 (97.1%)
Total	35 (100.0%)

Table 6: Bilirubin, Haemoglobin and Pcv Profile of the Study Population.

	Mean ± SD	Minimum	Maximum
Cord Blood Total Bilirubin	2.09 ± 0.40	0.62	3.92
Day 2 Total Bilirubin	10.59 ± 2.56	3.42	20.22
Day 5 Total Bilirubin	10.84 ± 2.76	5.52	21.2
Haemoglobin	15.68 ± 1.82	12.3	20.93
Day 2 Haemoglobin	14.54 ± 1.24	12.52	18.2
Day 5 Haemoglobin	14.75 ± 1.14	12.56	18.2
PCV	46.09 ± 4.46	38.6	58.6
Day 2 PCV	43.28 ± 3.38	34.5	55.6
Day 5 PCV	44.46 ± 2.69	39.2	51.3

Table 7: Comparative evaluations of cord, day 2 and day 5 total bilirubin, haemoglobin and PCV.

	Cord	Day 2	Day 5
Total Bilirubin	2.09 ± 0.40	10.59 ± 2.56	10.84 ± 2.76
Haemoglobin	15.68 ± 1.82	14.54 ± 1.24	14.75 ± 1.14
PCV	46.09 ± 4.46	43.28 ± 3.38	44.46 ± 2.69

Table 8: Diagnostic predictability of cord blood total bilirubin of >3 mg/dl for hyperbilirubinemia at 48 hours.

	Serum bilirubin (mg/ dl) at 48 hrs of life	
Cord bilirubin at birth (mg/dl)	≥15	<15
≥3	3	1
<3	0	70

Table 9: shows the diagnostic statistics.

Diagnostic Accuracy	TP	FP	FN	TN	PPV(%)	NPV(%)	Sensitivity(%	Specificity(%)
	03	01	00	70	68.6%	99.2%	98.4%	65.2%

circumstances, the umbilical cord serum indirect bilirubin is 1-3 mg/dl and rises at a rate of 5 mg/dl/day; thus, jaundice appears on the second or third day, usually peaking at 5-6 mg/dl between the second and fourth days and decreasing to 2 mg/dl between the fifth and seventh days of life.[10] [Table 5-7] Our hypothesis was that a high level of serum bilirubin at birth would indicate a high peak later in life. Our goal was to determine the connection between cord blood bilirubin and first-five-day peak serum bilirubin levels. We used cord blood estimation for initial serum bilirubin estimation since it is a simple and non-invasive method with results available shortly after birth.[11] oxytocin's function in hyperbilirubinemia- Oxytocin possesses anti-diuretic and anti-saluretic properties, causing hyponatremia and hypoosmolality in the mother. When oxytocin is given with an electrolyte-free dextrose solution, these metabolic alterations are exacerbated. This hypoosmolality is passed transplacentally to the foetus, causing increased osmotic fragility in red blood cells. The enlarged red blood cells in the spleen are easily damaged, resulting in an increase in bilirubin production [Table 4].[12,13] Early hospital release of babies resulted in a rise in occurrences of bilirubin-related brain impairment. As a result, having an accessible and safe test to identify babies who are at risk for substantial jaundice is critical, as it will aid in preventing a tragic outcome.[14] To address this problem, the American Academy of Pediatrics recommends that all newborns who were discharged within 48 hours of birth be followed up with within 2 to 3 days of discharge, either at the hospital, by a health care provider, or at home. Given the rarity of kernicterus and the difficulty of applying the advise, especially in lower socioeconomic and rural areas, documenting the advantages of this approach will be difficult.[15,16] Asking moms to look for yellowish discolouration (jaundice) in babies has not proven to be reliable. Many parents find it difficult to recognise serious jaundice despite such advice. Unfortunately, clinically, the appearance of severe jaundice for one's age is frequently overlooked, which means that there is no defined trigger for detecting the first serum bilirubin level and making a subsequent recommendation. This has the potential to be a significant issue. Jaundice arises in neonates at various intervals after birth, and the capacity to detect its severity, approximate range, and cephalocaudal progression has been a subject of research for more than 60 years. Furthermore, based on the height of TSB for age in hours at readmission, severe jaundice was very certainly present before the first hospital discharge in the majority of the previously reported healthy term neonates who developed kernicterus. Either the early icterus had gone unnoticed or the severity of the icterus for postnatal age was underestimated.[17,18] We now lack a viable mechanism for predicting such high levels of hyperbilirubinemia. Unfavorable outcomes can be avoided by following up regularly, closely, and frequently after birth and release from the hospital, but in rare cases of kernicterus, a more rigorous approach to newborn surveillance is required. Benefits, costs, practicality, and hazards of such a strategy must all be assessed. Umbilical cord blood collection is simple, painless, and requires no special equipment. The fact that test results are accessible within hours of birth is crucial. As a result, babies who are discharged within a few days of delivery can be evaluated for hyperbilirubinemia risk in a noninvasive fashion at birth. The use of cord blood bilirubin levels may help to identify babies at low risk of hyperbilirubinemia and avoid unnecessary hospitalisation.[19,20] With these considerations in mind, we conducted our research on healthy full-term newborns with non-hemolytic jaundice. Because specialised treatment is normally considered at or above this level, we have defined "hyperbilirubinemia" as a peak serum bilirubin level >15 mg/dl. Some neonatologists, however, start phototherapy at slightly lower levels of blood bilirubin, especially if they predict an increasing trend. As a result, we've forecast phototherapy as a treatment option. In diverse studies, the prevalence of hyperbilirubinemia ranges from 3.5 percent to 12.8 percent. Because our study group consisted of infants with no risk factors, the incidence of hyperbilirubinemia was 5.4 percent, which was the lowest among all studies.[21]

Other studies have found a link between higher levels of cord bilirubin and a higher risk of significant hyperbilirubinemia later in life. Raised cord blood bilirubin, whether ABO or non-

Table 10: Comparison of incidence of hyperbilirubinemia.

Studies	Year	No. Of Cases	Incidence of Hyperbilirubinemia
Palmer et al.	1983	41057	10.70
Phuapradit et al.	1993	7644	8.35
Awasthi et al.	1998	274	12.80
Alpay et al.	2000	498	12.05
Agarwal et al.	2002	213	10.30
Knupfer M et al.	2005	1100	10.60
Amar T et al.	2005	200	9.5
Randev S et al.	2010	200	12
Nilesh Ahire et al.	2014	113	3.5
Present Study	2020	74	5.4

ABO, indicates continued hemolysis in the mother's womb. Hyperbilirubinemia is more likely to occur in these babies. Hyperbilirubinemia could be predicted with a sensitivity of 100 percent, specificity of 98.17 percent, positive predictive value of 66.67 percent, and negative predictive value of 100 percent in the current study utilising serum bilirubin levels less than 3 mg/dL in cord blood.

Conclusion

Hyperbilirubinemia is one of the most common disorders found in postnatal wards. In 5-10% of healthy term newborns, neonatal hyperbilirubinemia develops. Up to 4% of term newborns are readmitted to the hospital during their first week of life, with jaundice accounting for around 85% of those readmitted. By causing hemolysis, oxytocin has the potential to cause neonatal hyperbilirubinemia, hence it should be taken with caution. The use of simple predictors to identify at-risk newborns for substantial hyperbilirubinemia can help to prevent bilirubin-induced neurological impairment. In healthy term babies (without RH and ABO incompatibility with Cord Blood Bilirubin 3mg/dl), a 99.2% Negative Predictive Value shows that cord serum bilirubin can aid to identify those newborns who are unlikely to require further examination and intervention. Babies with a cord blood bilirubin level of less than 3 mg/dl should be monitored more regularly to minimise newborn hyperbilirubinemia-related morbidity and mortality. There were no neonates in our study sample that were of the same age. This is where our research shines. It means that the Prediction test (48 hours TSB 15 mg/dl) that we developed can be used on neonates from the local rural community. As a result, predicting neonatal hyperbilirubinemia will have far-reaching implications, particularly in our rural setting.

References

1. Ullah S, Rahman K, Hedayati M. Hyperbilirubinemia in Neonates: Types, Causes, Clinical Examinations, Preventive Measures and Treatments: A Narrative Review Article. Iran J Public Health. 2016;45(5):558–568.
2. Olusanya BO, Osibanjo FB, Slusher TM. Risk factors for severe neonatal hyperbilirubinemia in low and middle-income countries: a systematic review and meta-analysis. PLoS One. 2015;10(2):0117229. Available from: https://doi.org/10.1371/journal.pone.0117229.
3. Penn AA, Enzmann DR, Hahn JS, Stevenson DK. Kernicterus in full term infant. Pediatrics. 1994;93:1003–1006.
4. Hansen TW. Kernicterus in a full-term infant: the need for in creased vigilance. Pediatrics. 1995;95(5):799–799.
5. Newman TB, Maisles MJ. Does hyperbilirubinemia damage the brain of healthy full-term infants? Clin Perinatol. 1990;17(2):331–358.
6. Maisles MJ, Newman TB. Kernicterus in Otherwise Healthy Breast-fed Term Newborns. Pediatrics. 1995;96:730–733.
7. Kaplan M, Hammerman C, Vreman HJ, Wong RJ, Stevenson DK. Hemolysis and Hyperbilirubinemia in ABO Blood Group Heterospecific Neonates. J Pediatr. 2010;157(5):772–777. Available from: https://dx.doi.org/10.1016/j.jpeds.2010.05.024.
8. Bahl L, Sharma R, Sharma J. Etiology of neonatal jaundice at Shimla. Indian Pediatr. 1994;31(10):1275–1278.
9. Murki S, Majumudhar S, Marwaha N, Narang A. Risk factors of Kernicterus in term babies with Non haemolytic Jaundice. Indian Pediatr. 2001;38(7):757–62.
10. Moyer VA, Ahn C, Sneed S. Accuracy of clinical judgment in neonatal jaundice. Arch Pediatr Adolesc Med. 2000;154(4):391–395. Available from: https://doi.org/10.1001/archpedi.154.4.391.
11. Seidman DS, Stevenson DK, Ergaz Z. Hospital readmis¬sion due to neonatal hyperbilirubinemia. Pediatrics. 1996;96:727–729.
12. 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. Available from: https://doi.org/10.1542/peds.114.1.297.
13. Bernaldo AJN, de Mattos Segre CA. Bilirubin dosage in cord blood: could it pre¬dict neonatal hyperbilirubinemia? Sao Paulo Med J. 2004;122(3):99–103. Available from: https://doi.org/10.1590/s1516-31802004000300005.
14. Knupfer M, Pulzer F, Gebauer C, Robel-Tillig E, Vogtmann C. Predictive value of umbilical cord blood bilirubin for postnatal hyperbilirubinaemia. Acta Paediatr. 2005;94(5):581–587. Available from: https://doi.org/10.1111/j.1651-2227.2005.tb01943.x.
15. Awasthi S, Rehman H. Early prediction of neonatal hyper¬bilirubinemia. Indian J Pediatr. 1998;65(1):131–139. Available from: https://doi.org/10.1007/bf02849704.
16. Alpay F, Sarici SU, Tosuncuk HD, Serdar MA, Inanc N, Gokcay E. The Value of First Day Bilirubin Measurement in Predicting the Development of Significant Hyperbilirubinemia in Healthy Term Newborns. Pediatrics. 2000;106(2):16. Available from: https://doi.org/10.1542/peds.106.2.e16.
17. Agarwal R, Deorari AK. Unconjugated Hyperbilirubinemia in Newborns: Current Perspective. Indian Pediatr. 2002;39:30–42.
18. Randev S, Grower N. Predicting neonatal hyperbilirubinemia using first day serum bilirubin levels. Indian J Pediatr. 2010;77(2):147–150. Available from: https://doi.org/10.1007/s12098-009-0335-3.
19. Bhutani VK, Johson L, Sivieri EM. Predictive ability of a predischarge hour specific serum bilirubin for subsequent significant hyperbilirubinemia in healthy term and near term newborns. Pediatrics. 1999;103(1):6–14. Available from: https://doi.org/10.1542/peds.103.1.6.
20. Gupta PC, Kumari S, Mullick DN. Icterometer; useful screening tool for neonatal jaundice. Indian Pediatr. 1991;28(5):473–476.
21. das Graças da Cunha Leite M, de Araújo Granato V, Facchini FP, Marba STM. Comparison of transcutaneous and plasma bilirubin measurement. J Pediatr. 2007;83(3):283–286. Available from: https://doi.org/10.2223/jped.1619.

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