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CAN CORD BLOOD BILIRUBIN BE USED AS PREDICTIVE MARKER FOR HYPERBILIRUBINEMIA IN NEWBORNS? A PROSPECTIVE STUDY

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ABSTRACT

Background: The most common causes of admission to hospital in the neonatal period is due to hyperbilirubinemia. Hyperbilirubinemia is a major contributor of morbidity in neonates. Prevention of serious complications is the main aim. Early discharge from the hospital which is widely seen now days might cause delay in recognition of hyperbilirubinemia. A remarkable biomarker identifier could be of real advantage and advancement. **Methods:** This study was undertaken to study weather cord blood bilirubin can be used as a predictor for hyperbilirubinemia. The study was taken up in the department of pediatrics of a tertiary teaching hospital. A total of 100 babies were taken for the study during the whole study period. The babies were examined and a detailed clinical examination was done at the time of birth and documented along with maternal history. The cord blood at the time of delivery and 48 hour serum blood was collected and sent to the lab for bilirubin level estimation. **Results:** The study consisted of 53 females and 47 males. Out of the 100 subjects 73 were caesarean and 27 were normal vaginal deliveries. With regard to term of gestation 72 babies were early term, 23 full-term and 5 late term. The mean cord bilirubin was 2.44mg/dl and the mean 48 hour serum bilirubin level was 13.12mg/dl. The incidence of hyperbilirubinemia in this study was 25%. The sensitivity was 35%, specificity was 75%, positive predictive value was 58.33%, negative predictive value 53.57%, false negative was 65% and false positive was 25%. Test for correlation was done between cord bilirubin and 48 hour serum bilirubin. There was moderate level ($r > 0.3$) of correlation which was highly significant ($p < 0.001$). **Conclusion:** This study concluded cord bilirubin can be used as a predictor for hyperbilirubinemia.

KEYWORDS: Hyperbilirubinemia, cord blood and 48 hour serum blood.

INTRODUCTION

The most common cause of admission to hospital in the neonatal period is due to hyperbilirubinemia.[1,2] Prevention of serious complications is the main aim. Early discharge from the hospital which is widely seen now days might cause delay in recognition of hyperbilirubinemia.[3,4] A remarkable biomarker identifier could be of real advantage and advancement. Few newborns show elevated bilirubin levels which can be a warning of brain damage.[5] Routinely physiological jaundice appears on the 2^{nd} – 3^{rd} day and elevated between 5^{th}-7^{th} day of life.[6] Jaundice is seen in 60% term and 80% pre term babies in a first week of life.[7] Cord bilirubin, routine investigations and 48 hour bilirubin will help estimate hyperbilirubinemia.[8] Many studies conducted have reported association between cord bilirubin and risk of hyperbilirubinemia.[9,10] Cord bilirubin as a marker or screening test has and is being discussed.[11,12] In the first week of life, bilirubin production increases and bilirubin elimination decreases causing total serum bilirubin to rise.[13] A major role is played by the placenta in bilirubin excretion in utero as the liver ability to metabolize bilirubin is slender.[14] The incidence of hyperbilirubinemia is 25.3% in pre term and 10.5% in term babies.[15] Notable neonatal hyperbilirubinemia is when the bilirubin levels >15mg/dl at 48 hours and 17mg/dl at 72 hours.[16] This study was conducted to estimate whether cord blood bilirubin level could predict subsequent hyperbilirubinemia among newborns.

AIM: To determine the predictive ability of cord bilirubin levels leading to hyperbilirubinemia in healthy term newborns.

OBJECTIVES

1. To estimate the incidence of hyperbilirubinemia
2. To assess the correlation between cord blood bilirubin and risk of neonatal hyperbilirubinemia (48 hour serum bilirubin).

Study design: Prospective study

Study setting: The study was conducted in the Department of Paediatrics at Aarupadai Veedu Medical College and Hospital, Puducherry**.**

Study population: Newborn babies born to mothers delivered in Aarupadai Veedu Medical College and Hospital, Puducherry**.**
Study duration: October 2018 to September 2020.

Inclusion Criteria
1. Term babies (>37 completed weeks) of both gender delivered at Aarupadai Veedu Medical College and Hospital.
2. Modes of delivery – normal vaginal delivery / cesarean section
3. Birth weight:- > 2.5 to 4 kg.
4. Small for gestational age

Exclusion Criteria
1. Newborn <37 weeks of gestation.
2. At risk of sepsis
3. Instrumental delivery (vacuum and forceps)
4. Birth asphyxia
5. Newborn with obvious IUGR.
6. Visible congenital anomalies and still birth.
7. Meconium stained amniotic fluid.
8. Newborn with APGAR score <7/10 at 1 & 5 minutes.
9. Babies discharge prior to 72 hours.

Sample Size
Considering the prevalence of neonatal hyperbilirubinemia as 55.2%in a study by Hanneke B et al [17] the sample size was calculated for our study using the formula
$N = 4pq/L^2$:
- p= 55.2%
- q= 44.8 (100-p)
- L=20%

Sample size works out to 80 subjects with the above formula and the study was rounded off to 100 subjects.

Study procedure: Babies were clinically assessed for age, sex, gestational age, birth weight, previous history of jaundice in the family, day of onset of jaundice, pattern of feeding, fever and other neurological symptoms. A complete clinical examination of the baby was also carried out. 2ml of blood was drawn in a sterile manner from the umbilical cord & veni-puncture on subsequent analysis at 24hours and 48 hours of life from neonates. All these samples were sent with sterile disposable syringes & needle. The test tubes contained ethylene diamine tetra acetic acid (EDTA) & they were taken to the lab immediately.

Data collection tools: All the relevant parameters were documented using a structured proforma. The Proforma contained the following details
1. Demographic parameters – like age, gender etc.
2. Medical illness – Fever and other comorbid illness
3. All Baseline parameters were checked (Pulse, BP, height, weight, BMI)
4. Clinical examination findings

Operational definitions
- Cord bilirubin cut off at > 2.5mg/dl[18] and 48 hour serum bilirubin cut off at > 15mg/dl.[18]

Ethical Issues
Ethical clearance was obtained from the Institutional human ethical committee. Informed consent was obtained from each study participant, after explaining the risks and benefits involved in the study and voluntary nature of the participation, in a language participant could understand. Confidentiality of the study participants was maintained throughout the trial conduction and dissemination of the study results.

Data entry and analysis
- The collected data was coded, entered into Microsoft excel work sheet and exported to SPSS. Data was analyzed using SPSS version 21. Data is presented as percentage in categories and then presented as tables and graphs. Pearson test for correlation was used for test of significance.

RESULTS

Table 1: Distribution of subjects

Variable	Frequency	Percent
Sex		
Males	47	47
Females	53	53
Mode of delivery		
Vaginal delivery	27	27
Caesarean section	73	73
Gestational age		
Early term	72	72
Full term	23	23
Late term	5	5
Bilirubin levels	**Minimum**	**Maximum**
Cord bilirubin levels	1.1 mg/dl	9.8 mg/dl

Mean cord bilirubin level	2.44 mg/dl	
48 hour bilirubin	4.3 mg/dl	22.4 mg/dl
Mean 48 hour bilirubin level	13.12 mg/dl	
Significant jaundice	**Frequency**	**Percent**
Incidence	25/100	25%
Evaluation results		
Sensitivity		35%
Specificity		75%
Positive predictive value		58.3%
Negative predictive value		53.57%
False negative		65%
False positive		25%

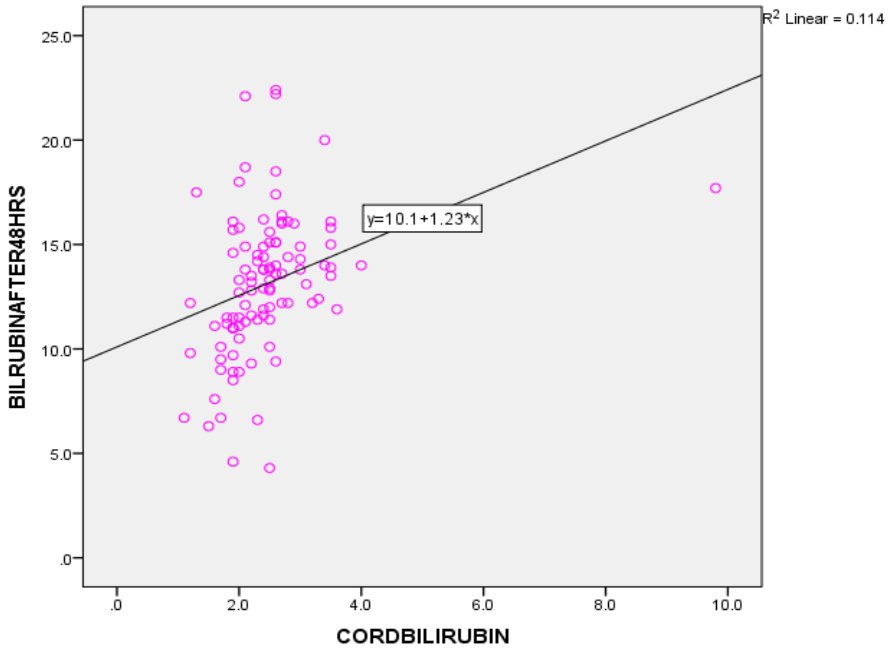

Figure 1: Correlation between cord and 48 hour bilirubin levels.

The present study consisted of 53 females and 47 males. Out of the 100 subjects 73 were caesarean and 27 were normal vaginal deliveries With regard to term of gestation 72 babies were early term, 23 full-term and 5 late term. The mean cord bilirubin was 2.44mg/dl and the mean 48 hour serum bilirubin level was 13.12mg/dl. The cut off level was 2.5mg/dl for cord bilirubin and 15mg/dl for 48 hour serum bilirubin. The incidence of hyperbilirubinemia in this study was 25%. Screening tests were done to estimate weather cord bilirubin can be used as predictor for hyperbilirubinemia. The sensitivity was 35%, specificity was 75%, positive predictive value was 58.33%, negative predictive value 53.57%, false negative was 65% and false positive was 25%. Test for correlation was done between cord bilirubin and 48 hour serum bilirubin. There was moderate level ($r>0.3$) of correlation which was highly significant ($p<0.001$).

DISCUSSION

An observational study conducted by Nilesh, Ravindra et al[19] also had sample size (113) close to the present study where their study consisted of 57 males and 56 females. A .M. Jukic et al[20] in their study found the median time from ovulation to birth was 268 days. Co-efficient of variation is higher when LMP is measured i.e 49% than by ovulation which was 3.7%. Conceptions which took longer to implant took longer to delivery. Mothers with longer gestations were older had longer pregnancies and babies were heavier at birth.

The present study showed early term of higher percentage followed by full term and late term. In our study out of the 100 subjects 27 subjects were normal deliveries and breast feeding was initiated within 30 minutes post-delivery. Studies by Kannan R.[21] among 300 subjects the mean cord bilirubin was 2.04mg/dl quite similar and closer means of 2.44mg/dl were observed in the present study also the mean 48 hour serum bilirubin was 9.08mg/dl whereas in this study the mean was 13.12mg/dl. The study conducted by Nilesh A[19] suggested the mean 48 hour serum bilirubin of 10.58mg/dl. Study by Zakia N.[18] in their study took the cord bilirubin cutoff at 2.5mg/dl and proceeded with the study. Similarly in this study also cord bilirubin level was taken at a cut of 2.5mg/dl.

Knudsen et al[22] took the 48 hour serum bilirubin cutoff at 15mg/dl. The present study also we have kept the 48 hour bilirubin cutoff at 15mg/dl. Study in 2010 by Ramdev et al[23] suggested an incidence rate of 12% among 200 subjects. Knupfer et al[24] also conducted similar studies and projected an incidence rate of 10.60% among 1100 babies in the year 2005.

A study done by Kannan R.[21] among 300 subjects projected sensitivity of 92.3%, specificity of 71.16%, positive predictive value of 23.3% and negative predictive value of 98.98%. The present study projected a sensitivity of 35%, specificity of 75% and positive predictive value of 58.33% and negative predictive value of 53.57%. The percentage of evaluation is lesser because of a smaller sample size. A study in 2007 conducted by Sun et al.[25] showed a sensitivity of 68% and positive predictive value of 45.8%.

The study carried by Kannan R.[21] concluded that cord bilirubin of $\geq$ 2.15 mg/dl can be used as a predictor of neonatal hyperbilirubinemia. Similar finding were seen in our study too were the cord bilirubin level above 2.5mg/dl resulted in hyperbilirubinemia in the first two days of life. Nilesh A et al[19] also concluded in their study that increased levels of cord bilirubin can be used as an indicator for neonatal hyperbilirubinemia.

CONCLUSION

This study concluded the incidence rate of hyperbilirubinemia was 25% and cord blood can be used a used a marker for neonatal hyperbilirubinemia.

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