Association of cord serum albumin with neonatal hyperbilirubinemia among term appropriate-for-gestational-age neonates

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Abstract

Introduction: Neonatal jaundice affects nearly 60% of term and 80% of preterm neonates during the first week of life. Although early discharge of healthy term newborns is a common practice, neonatal hyperbilirubinemia (NH) is the most common cause for readmission during the early neonatal period.

Objective: To determine the association of cord serum albumin with serum bilirubin levels and whether it can be used as a risk indicator for the development of NH.

Method: In this observational study, cord blood was collected from healthy term newborns for serum albumin level measurements. Total serum bilirubin and direct serum bilirubin were measured during 72–96 h of life. Newborns were clinically assessed daily for NH or for any other complication during the study period.

Result: Among the study cohort of 300 babies, 35 had a total serum bilirubin level ≥17 mg/dl after 72 h and were considered to have NH. They were grouped as Group 1, Group 2, and Group 3 according to the cord serum albumin level ≥2.8 g/dl, 2.9–3.3 g/dl, and ≥3.4 g/dl, respectively. Statistical analysis was conducted to assess the correlation of cord serum albumin with NH. The results showed that a cord serum albumin level ≥2.8 g/dl is critical, as it was seen in 95% of term newborns who developed NH. In the group where cord serum albumin was ≥3.4 g/dl, none of the term newborns developed NH.

Conclusion: Term neonates with hyperbilirubinemia with a total serum bilirubin level ≥17 mg/dl had levels of cord serum albumin of ≥2.8 g/dl, and this can be used as a risk indicator to predict the development of NH.

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1. Introduction

Jaundice in the neonatal period is a common finding during the first few days after birth. Approximately 3% of healthy newborns develop jaundice with a serum bilirubin level of 15 mg/dl or higher. Neonatal hyperbilirubinemia (NH) is a cause of concern for both pediatricians and parents [1]. The concept of prediction offers an attractive option to identify babies at risk of developing NH in institutions where healthy newborns are discharged within 24–48 h of birth. Clinical examination is suggestive, but to have a diagnosis of significant jaundice, serum bilirubin estimation is necessary. If the newborns at risk of developing hyperbilirubinemia are identified at the time of delivery, then an appropriate plan of management can be advised for follow-up. Phototherapy can be started early in this group of babies more effectively.

Human and animal fetuses can synthesize albumin endogenously from early fetal life, starting at approximately the seventh week of intrauterine life. Fetal liver in preterm babies can synthesize albumin, but they still present with hypoalbuminemia [2]. In term babies, a serum albumin level of 2.8 g/dl is considered the lower limit of the acceptable range [3]: mean serum albumin level at term is 3.1 g/dl [4] and the normal range of serum albumin level at term is 3.1 ± 3 g/dl.

2. Aim of the study

The study was devised to determine the association between various levels of cord serum albumin (CSA) and serum bilirubin necessitating interventions in the form of exchange transfusion or
phototherapy and whether it can be used as a risk indicator for subsequent development of significant jaundice.

3. Materials and method

The present study was conducted in the neonatal unit of a large industrial hospital in the eastern part of India. Three hundred healthy term newborns, delivered in the hospital between February 2015 and October 2015, were considered for inclusion in the study. The study had obtained approval from the institutional research and ethics committee.

3.1. Inclusion and exclusion criteria

Term babies of both genders delivered both normally or by caesarean section, with birth weight ≥2.5 kg and an Apgar score of ≥7/10 at 1 min, were included. All other babies, who were at more risk of developing jaundice because of their clinical status, were excluded. Babies with prematurity, Rh-negative mother, sepsis, meconium aspiration syndrome, breathing difficulty, meconium aspiration syndrome, first day jaundice, cephalohematoma, diabetic mother, and twin to twin transfusion were excluded.

3.2. Collection of data

Parents of these babies were informed about the study, and their consent was obtained for each baby before enrolling them in the study. Demographic profile and relevant information was collected using a structured proforma, which was prepared, and information was gathered by talking to the mother and from the mother's case sheet. Gestational age was determined by Ballard scoring and from the mother’s last menstrual period. The CSA level was estimated at birth, and the serum bilirubin level was estimated at 72 h of life. These babies were clinically evaluated for jaundice every day during their nursery stay, subsequently. The serum albumin level was estimated from 2 ml of cord blood sample collected from the placental end, after its separation. Venous blood samples were collected from the baby at 72–96 h of life and analyzed for total and direct serum bilirubin and blood group.

3.3. Inference

The study outcome was designed to assess NH in newborns with a serum bilirubin level of ≥17 mg/dl after 72 h of life. American Academy of Pediatrics Practice Parameter 2004 [5] and IAP-NNF recommend phototherapy for that level of bilirubin [6].

4. Observation

This study was conducted on a total of 300 newborns. Individual proforma was filled for each newborn. Thirty-five neonates required intervention in the form of phototherapy. The data were analyzed using online calculators, http://vassarstats.net/odds2x2.html, and https://www.socscistatistics.com/tests/chisquare2/Default2.aspx.

A comparison between the newborns developing significant NH requiring phototherapy and cord albumin groups is shown in Table 1. The observation was statistically significant, with a P value <.00001.

The correlation of variables such as gender, mode of delivery, oxytocin, and cord albumin level with newborns developing significant NH requiring phototherapy is shown in Table 2. Statistical significance was not observed in any of these variables.

CSA levels and NH were studied for any statistical association and diagnostic predictability, and the results are shown in Table 3.

5. Discussion

NH is one of the common causes of readmissions of newborns who were discharged early after birth and not brought back by parents for follow-up during the next 24–48 h. There are recommendations for preterm and high-risk babies, which necessitate prolonged stay in the neonatal care unit, thus facilitating the identification of icterus and timely intervention. Identification of term healthy neonates, who may develop hyperbilirubinemia later, will help in withholding their discharge from hospital or insisting on an early follow-up visit during the next 24–48 h, thereby facilitating optimal management of NH. We tried to assess the albumin level in the cord blood as a screening tool for assessing the risk of subsequent development of NH.

The incidence of NH was found as 11.5%. In the present study, variables such as gender of the baby, mode of delivery, and oxytocin induction of labor did not have significant association with subsequent development of NH. Observations were similar to those reported in the studies by Sahu et al., in 2011 and Trivedi et al., in 2013, with statistically significant association between a CSA level of <2.8 g/dl and subsequent development of NH.

Newborns in the group with CSA <2.8 g/dl were further analyzed statistically, with emphasis on sensitivity, negative predictive value (NPV), Odds ratio (OR), 95% CI, and risk ratio (RR). With a sensitivity of 94%, NPV of 98.8%, OR of 27.66, and RR of 21, a CSA of <2.8 g/dl has a good predictive value for subsequent development of NH. These studies are compared in Table 4.

The observations of Sahu et al. [7] and Trivedi et al. [8] were similar for the association of CSA with NH.

Thus, the CSA level appears to have a predictive value in NH. This study indicates that a CSA level <2.8 g/dl can be considered as a factor for the subsequent development of significant jaundice and a level of ≥3.4 g/dl is safe for early discharge in the absence of other risk factors.

6. Conclusion

Healthy full-term newborns with NH had levels of CSA of ≤2.8 g/dl. Therefore, this value can be used as a risk indicator for the prediction of subsequent development of significant jaundice, whereas a CSA level of ≥3.4 g/dl can be considered safe.
Table 2
Correlation of clinical variables with need for phototherapy.

| Variables            | Phototherapy |
|----------------------|--------------|
|                      | No n = 265 (%) | Yes n = 35 (%) |
| Gender               |              |               |
| Male                 | 150 (56.5)   | 19 (55)       |
| Female               | 115 (43.5)   | 16 (45)       |
| Mode of delivery     |              |               |
| Cesarean             | 77 (29.2)    | 10 (30)       |
| Normal vaginal       | 188 (70.8)   | 25 (70)       |
| Oxytocin drug use    |              |               |
| No                   | 101 (38.8)   | 16 (45)       |
| Yes                  | 164 (61.2)   | 19 (55)       |

Table 3
Diagnostic predictability of cord serum albumin levels for neonatal hyperbilirubinemia.

| Variables          | Sensitivity % | Specificity % | PPV | NPV | Odds ratio (OR) 95% CI with range | Risk ratio (RR) 95% CI with range |
|--------------------|---------------|---------------|-----|-----|-----------------------------------|---------------------------------|
| Cord albumin <2.8 g/dl | 94            | 62.44         | 25  | 98.8| 27.66, 6.497–117.81               | 21, 5.13–5.952                   |
| Cord albumin 2.9–3.3 g/dl | 5.0          | 63.7          | 2   | 83.6| 0.106, 0.025–0.454                | 0.124, 0.03–0.51                |
| Cord albumin >3.4 g/dl  | 0.00          | 73.5          | 0.00| 84.7| 0                                  | 0                               |

Table 4
Comparison of CSA level as a risk indicator for NH in other studies.

| Studies            | Year | Total no. of patients | No. of patients with NH | Cord albumin correlation with NH | P value |
|--------------------|------|-----------------------|-------------------------|---------------------------------|---------|
| Sahu et al. [7]    | 2011 | 40                    | 20                      | 14 (<2.8 g/dl) 6 (2.9–3.3 g/dl) 0 (>3.4 g/dl) | <.001   |
| Trivedi et al. [8] | 2013 | 605                   | 205                     | 120 (<2.8 g/dl) 59 (2.93.3 g/dl) 26 (>3.4 g/dl) | <.05    |
| Present study      | 2015 | 300                   | 35                      | 33 (<2.8 g/dl) 2 (2.9–3.3 g/dl) 0 (>3.4 g/dl) | <.00001 |

Funding
This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Declaration of interest
None.

Ethical statement
This work was carried out in accordance with International Code of Medical Ethics of the World Medical Association (Declaration of Helsinki) for experiments involving humans. Informed consent from parents was obtained before inclusion of the babies in the studies.

Author agreement
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Credit authorship contribution statement
Asit Kumar Mishra: Conceptualization, Methodology, Data curation, Supervision, Validation, Writing - review & editing. C. Sanyasi Naidu: Formal analysis, Investigation, Writing - review & editing.

Acknowledgment
The authors acknowledge the contribution from Dr Keshav Kumar of the Department of Beverage Research, Hochschule Geisenheim University, Geisenheim, Germany, for his contribution in statistical analysis used in the manuscript. They are thankful to GM Medical Services, Tata Main Hospital, Tata Steel, for providing permission to submit the manuscript for publication.

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