MAK HILL Publications Research Journal of Medical Sciences

Research Article
doi: 10.59218/makrjms.2023.12.104.110

# Assessment of Cord Bilirubin, Total Serum Bilirubin and Transcutaneous Bilirubin for Predicting and Managing Neonatal Jaundice

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**ABSTRACT**

Neonatal jaundice, characterized by yellowing of the skin and mucous membranes due to elevated bilirubin levels, is a common clinical sign in newborns. Effective management of jaundice is essential to reduce morbidity and mortality rates. However, the rising costs of healthcare and the trend toward shorter post-delivery hospital stays necessitate early identification and risk assessment of neonatal jaundice. Unidentified hyperbilirubinemia can lead to severe complications, such as Bilirubin Induced Neurological Dysfunction (BIND). In this context, our study aimed to explore the predictive potential of cord bilirubin (CB), transcutaneous bilirubin (TcB) and total serum bilirubin (TSB) in neonatal jaundice management, focusing on a rural hospital's need for efficient early discharge strategies while minimizing complications. Implement a third-day discharge policy for neonates at minimal risk, coupled with regular check-ups. Enforce early follow-up within 48 hrs for neonates at moderate risk. Initiate prompt interventions for high-risk neonates. Identify potential causative factors contributing to neonatal hyperbilirubinemia. A prospective cohort of 650 consecutive live newborns was studied. Neonates were evaluated for jaundice at birth (cord bilirubin), between 24-72 hrs (transcutaneous bilirubin, TcB, using Kramer's rule and after 72 hrs (total serum bilirubin, TSB and TcB). Exclusion criteria included extreme prematurity, low birth weight, multiple gestation, life-threatening congenital anomalies, severe birth asphyxia, conjugated hyperbilirubinemia, jaundice onset after two weeks and Rh incompatibility. The study revealed a positive correlation between cord bilirubin and TSB at 72 hrs, as well as between cord bilirubin and TcB at 72 hrs. Cord bilirubin levels exceeding 2.5 mg $dL^{-1}$ exhibited a high sensitivity (78.18%) and negative predictive value (86.66%) for predicting significant hyperbilirubinemia. Analysis by weight groups showed that cord bilirubin, TSB and TcB were effective determinants in predicting hyperbilirubinemia. TcB measurements demonstrated a significant correlation with TSB levels, strengthening their use in identifying neonates at risk. This study presents critical insights into neonatal jaundice management in a rural hospital setting. The predictive power of cord bilirubin, TSB and TcB can improve risk-based discharge and follow-up strategies, reducing complications associated with hyperbilirubinemia.

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**Key Words**
Cord bilirubin, transcutaneous bilirubin, neonatal jaundice, bilirubin levels

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**Received:** 28 September 2023
**Accepted:** 10 October 2023
**Published:** 19 October 2023

**Citation:** Parikshit Pundalik Deore, Abhinay Bhaskar Darwade and Sunil Dhansing Pagare, 2023. Assessment of Cord Bilirubin, Total Serum Bilirubin and Transcutaneous Bilirubin for Predicting and Managing Neonatal Jaundice. Res. J. Med. Sci., 17: 104-110, doi: 10.59218/makrjms.2023.12.104.110

## INTRODUCTION

Over the last several decades the rapid advances in neonatal care have resulted in significant reduction in morbidity and mortality[1-3].

Jaundice related morbidity has been minimized by vigilant observation, early detection and early institution of effective and intensive phototherapy. Jaundice, defined as yellow discoloration of skin and mucous membranes due to chemical hyperbilirubinemia, is a common clinical sign in newborns. Though often normal (physiologic), could be pathologic and hence of concern to both the treating physician and the parents[2-5]. With the spiraling cost of medical care, in particular, hospitalization of the parturient mother and newborn as well as the limitation on hospital beds the need for early discharge has been felt. Failure to identify the presence and the severity of jaundice in the newborn can lead to complications of unconjugated hyperbilirubinemia i.e. BIND. (Bilirubin induced neurological dysfunction)[6]. Thus, along with the recent trend towards shorter post delivery hospital stay, an increase in complications from hyperbilirubinemia is expected[7]. Hence it becomes necessary for the primary care physician to be on the lookout for newborns at risk so that he may coordinate parent education, estimate serum bilirubin levels in relation to gestational age, birth weight, mother's and baby's blood group.

Neonatal jaundice is one of the most upcoming topics in today's medical field. It has been tackled very well in most developed countries. The purpose of my dissertation is to predict the possibility of significant hyperbilirubinemia in newborns on the basis of cord bilirubin (CB), transcutaneous bilirubin (TcB) and total serum bilirubin (TSB) so as to decide eligibility for early discharge or otherwise[8,9].

Advantages of TcB are that it is noninvasive, cost beneficial, not painful to the newborn and hence compliance expected from the parents ,time saving, accurate with easy handling and having good correlation with TSB before starting phototherapy[10,11]. Advantages of Cord Bilirubin (CB) are that it is easy to collect, non-invasive, without blood loss to neonate and allows earlier reporting of blood group and baseline bilirubin .

In recent decades, significant progress in neonatal care has led to a notable decrease in both the illness and mortality rates among newborns. This progress includes the effective management of jaundice, which is characterized by yellowing of the skin and mucous membranes due to elevated bilirubin levels[10,11]. Jaundice is a common occurrence in newborns and while it is often a normal physiological process, it can sometimes signal underlying health concerns, raising both medical and parental worries. The increasing costs of medical care, particularly hospitalization for mothers and newborns, combined with limited hospital bed availability, have prompted the desire for earlier discharges. Failing to identify and assess jaundice promptly in newborns can lead to complications associated with unconjugated hyperbilirubinemia, such as Bilirubin Induced Neurological Dysfunction (BIND)[12,14]. As a result, as the trend moves toward shorter post-delivery hospital stays, it is expected that complications related to hyperbilirubinemia may increase. Therefore, it is crucial for primary care physicians to be vigilant in identifying at-risk newborns. This allows them to coordinate parental education, estimate serum bilirubin levels relative to factors like gestational age, birth weight and the mother's and baby's blood group. [15]

Neonatal jaundice is a prominent topic in today's medical field, having been well-addressed in many developed nations. The objective of my dissertation is to predict the likelihood of significant hyperbilirubinemia in newborns by analyzing cord bilirubin (CB), transcutaneous bilirubin (TcB) and total serum bilirubin (TSB)[16]. This prediction aids in deciding whether early discharge is appropriate. The advantages of using TcB include its non-invasive nature, cost-effectiveness, lack of pain for the newborn, thus ensuring parental cooperation, time efficiency, accuracy, ease of use and a strong correlation with TSB before initiating phototherapy[16].

Cord Bilirubin (CB) has its own merits, as it is easy to collect, non-invasive, causes no blood loss to the newborn and allows for earlier reporting of blood group and baseline bilirubin levels.

### Aim and objectives

**Aim:** To establish the link between Cord bilirubin, TcB and TSB levels in neonates delivered at a rural hospital and formulate a discharge strategy tailored to the risk of unconjugated hyperbilirubinemia.

**Objectives:** Implementing a third-day discharge policy coupled with regular check-ups for neonates at minimal risk.

- Enforcing early follow-up, within 48 hrs, for neonates at moderate risk
- Initiating prompt interventions for neonates deemed high risk
- Identifying potential causative factors contributing to neonatal hyperbilirubinemia.

## MATERIALS AND METHODS

All neonates in born the rural hospital will be evaluated for jaundice:

- At birth (cord)
- 24-72 hrs (TcB kramers)
- After 72 hrs (TSB.TcB, Kramers)

**Exclusion criteria:**

- Extreme prematurity (<28 weeks gestation)
- Low birth weight (LBW<2000 g)
- Multiple gestation
- Neonates with life threatening congenital anomalies
- Neonates with severe birth asphyxia
- Conjugated hyperbilirubinemia
- Onset of jaundice after 2 weeks of age
- Rh incompatibility
- Rh negative mothers

**Methods:**

- A printed questionnaire will be used to elicit detailed maternal history
- A printed Performa for recording thorough clinical examination of newborn including visual screening for neonatal jaundice using Kramer's rule will be used
- Investigations will include Cord bilirubin, total serum bilirubin (TSB), transcutaneous bilirubin (TCB) and others as indicated

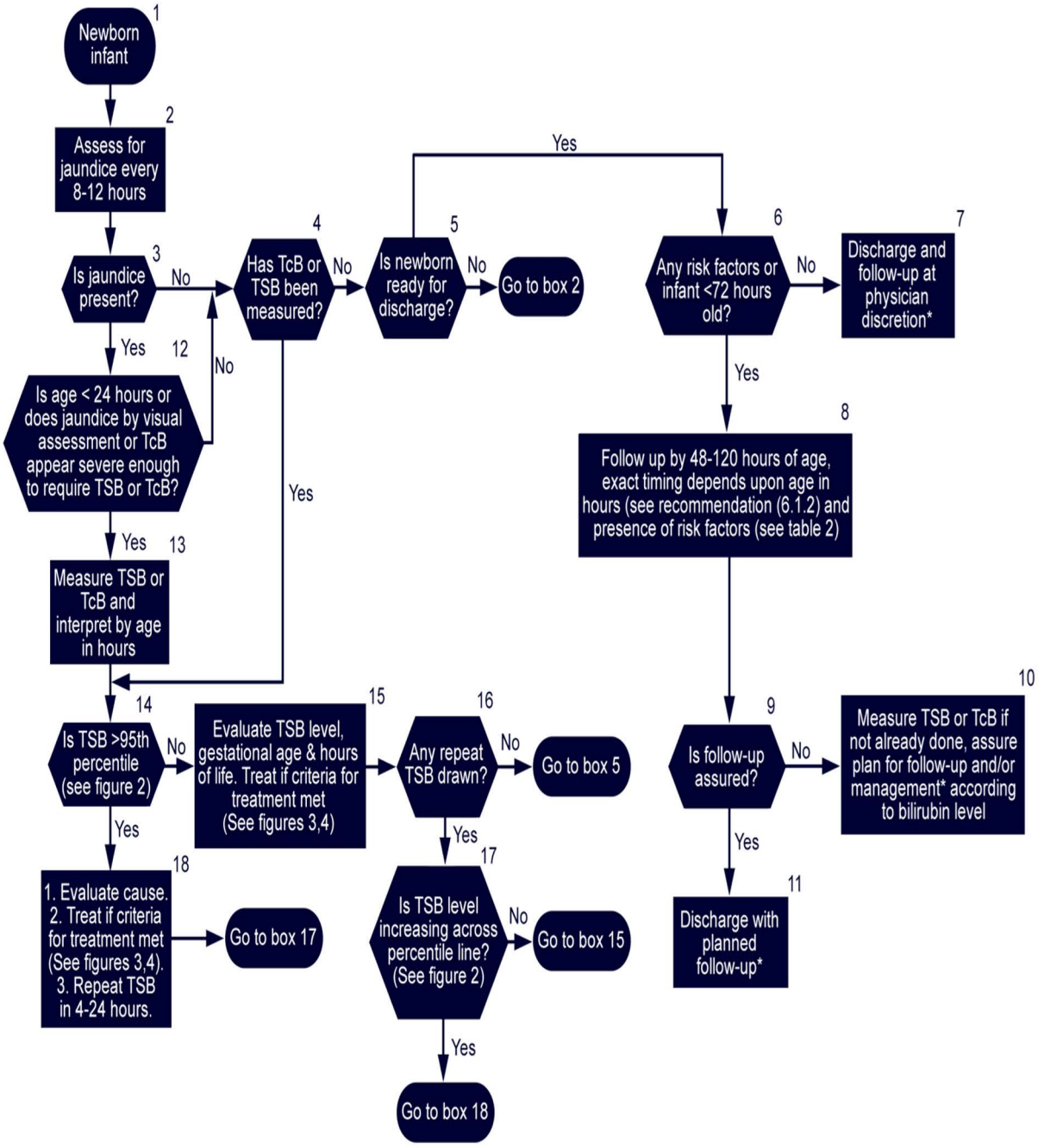


Fig. 1: Provide information and written guidelines about jaundice to parents of all newborns at discharge

Table 1: Predictive values of Mean cord bilirubin, TSB at 72 hrs age and TcB at 72 hrs age

| | Birth weight (mgs) | | | | | |
|---|---|---|---|---|---|---|
| | 2000-2500 | | 2500-3000 | | 3000-3500 | |
| Variables | Sr. Bilirubin =13.5 | Sr. Bilirubin >13.5 | Sr. Bilirubin =13.5 | Sr. Bilirubin >13.5 | Sr. Bilirubin =13.5 | Sr. Bilirubin >13.5 |
| Mean cord bilirubin | 2.02 | 2.76 | 2.54 | 2.85 | 1.62 | 2.91 |
| TSB at 72 hrs | 8.4 | 15.2 | 10.8 | 16.7 | 11.3 | 18.3 |
| TcB at 72 hrs | 10.8 | 12.4 | 11.6 | 16.6 | 12.5 | 19.6 |

## RESULTS

On considering Serum bilirubin level 13.5 as a cut off value for hyperbilirubinemia the entire sample size as per weight groups was observed for the serum bilirubin levels whether <13.5 or 0.13.5 and the mean cord bilirubin, mean 72 hrs TSB, mean 72 hrs TcB were correlated with the cut off value of 13.5. It was found that in the weight group of 2000-2500 g mean cord bilirubin was 2.02, mean TSB was 0f 8.4 and mean TcB of 10.8 when serum bilirubin was ≤13.5 whereas the mean cord bilirubin was 2.76, mean TSB was 15.2 and mean TcB was 12.4 when the serum bilirubin had crossed the cut off value of 13.5 (Table 1).

In the weight group of 2500-3000 g mean cord bilirubin was 2.54, mean TSB was 0f 10.8 and mean TcB of 11.6 when serum bilirubin was below the cut off value (≤13.5) whereas the mean cord bilirubin was 2.85, mean TSB was 16.2 and mean TcB was 16.6 when the serum bilirubin had crossed the cut off value of (>13.5).

` In the weight group of 3000-3500 g mean cord bilirubin was 1.62, mean TSB was 0f 11.3 and mean TcB of 12.5 when serum bilirubin was below the cut off value (≤13.5) whereas the mean cord bilirubin was 2.91, mean TSB was 18.3 and mean TcB was 19.6 when the serum bilirubin had crossed the cut off value of (>13.5). the above findings are highly suggestive that cord bilirubin, TSB and TcB are very useful determinants in early prediction of hyperbilirubinemia (Table 2).

In the weight group of 2000-2500 g the newborns who received phototherapy had a mean cord bilirubin of 2.76±0.52, mean TSB at 72 hrs of age of 16.95±3.11, mean TcB at 72 hrs of age of 13.59±1.86, TSB at 7th day of life 10.07±1.88, TcB at 7th day of life 4.53±2.07 and peak bilirubin of 16.62±2.59.

The newborns who did not receive phototherapy had a mean cord bilirubin of 1.92±0.41, mean TSB at 72 hrs of age of 10.71±0.41, mean TcB at 72 hrs of age of 10.48±1.53 TSB at 7th day of life 8.80±1.64 ,TcB at 7th day of life 4.01±2.12 and peak bilirubin of 8.19±3.02.

By applying Z test for difference between two sample means there is a highly significant difference between mean values of all characteristics in the above table for birth weight in between 2000-2500 g with respect to phototherapy given and not given. (i.e. p<0.01) (Table 3).

Table 2: Distribution of mean and SD values for various characteristics for babies with birth weight 2000-2500gms in respect to phototherapy given and not given

| Characteristics | Phototherapy Mean±SD | No phototherapy Mean±SD |
|---|---|---|
| Cord bilirubin | 2.76±0.52 | 1.92±0.41 |
| TSB at 72 hrs | 16.95±3.11 | 10.71±0.41 |
| TcB at 72 hrs | 13.59±1.86 | 10.48±1.53 |
| TSB at 7th day | 10.07±1.88 | 8.80±1.64 |
| TcB at 7th day | 4.52±2.07 | 4.01±2.12 |
| Peak bilirubin | 16.62±2.59 | 8.19±3.02 |

Table 3: Distribution of mean and SD values for various characteristics for babies with birth weight 2500-3000 g in respect to phototherapy given and not given

| Characteristics | Phototherapy Mean±SD | No phototherapy Mean±SD |
|---|---|---|
| Cord bilirubin | 2.62±0.61 | 2.17±0.46 |
| TSB at 72 hrs | 14.04±1.69 | 10.21±3.05 |
| TcB at 72 hrs | 12.81±1.78 | 10.65±1.00 |
| TSB at 7th day | 5.65±1.027 | 5.12±0.96 |
| TcB at 7th day | 4.29±1.09 | 4.12±0.98 |
| Peak bilirubin | 13.04±2.51 | 12.25±1.74 |

Table 4: Distribution of Mean and SD values for various characteristics for babies with birth weight 3000-3500 g in respect to phototherapy given and not given

| Characteristics | Phototherapy Mean±SD | No phototherapy Mean±SD |
|---|---|---|
| Cord bilirubin | 2.44±0.64 | 2.11±0.41 |
| TSB at 72 hrs | 13.64±1.78 | 10.04±2.96 |
| TcB at 72 hrs | 11.84±1.86 | 10.21±1.02 |
| TSB at 7th day | 5.45±0.96 | 5.09±0.78 |
| TcB at 7th day | 4.16±1.26 | 4.10±0.87 |
| Peak bilirubin | 12.98±2.02 | 12.20±1.38 |

In the weight group of 2500-3000 g the newborns who received phototherapy had a mean cord bilirubin of 2.62±0.61, mean TSB at 72 hrs of age of 14.04±1.69 , mean TcB at 72hrs of age of 12.81±1.78, TSB at 7th day of life 5.65±1.027, TcB at 7th day of life 4.29±1.09 and peak bilirubin of 13.04±2.51.

The newborns who did not receive phototherapy had a mean cord bilirubin of 2.17±0.46, mean TSB at 72 hrs of age of 10.21±3.05, mean TcB at 72 hrs of age of 10.65±1.00 TSB at 7th day of life 5.12±0.96, TcB at 7th day of life 4.12±0.98 and peak bilirubin of 12.25±1.74.

By applying Z test for difference between two sample means there is a highly significant difference between mean values of all characteristics in the above table for birth weight in between 2500-3000 gms with respect to phototherapy given and not given. (i.e. p<0.01) (Table 4).

In the weight group of 3000-3500 g the newborns who received phototherapy had a mean cord bilirubin of 2.44±0.64, mean TSB at 72 hrs of

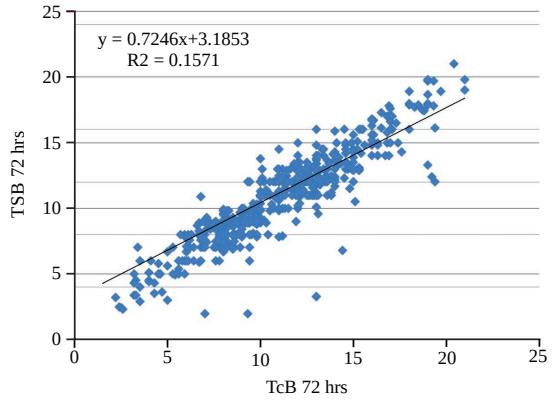


Fig. 2: Relationship Between Paired Bililcheck TcB Versus TSB Values For The Entire Study Population(N = 650). The Linear Regression Shoes A Significant Correlation

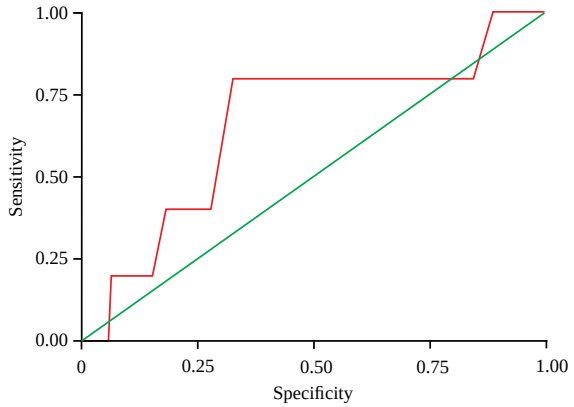


Fig. 3: ROC of third day bilirubin

age of 13.64±1.78, mean TcB at 72hrs of age of 11.84±1.04, TSB at 7th day of life 5.45±0.96, TcB at 7th day of life 4.16±1.26 and peak bilirubin of 12.98±2.02.

The newborns who did not receive phototherapy had a mean cord bilirubin of 2.11±0.41 mean TSB at 72 hrs of age of 10.04±2.96, mean TcB at 72hrs of age of 10.21±1.02, TSB at 7th day of life 5.09±0.78,TcB at 7th day of life 4.10±0.87 and peak bilirubin of 12.20±1.3.

By applying Z-test for difference between two sample means there is a highly significant difference between mean values of all characteristics in the above table for birth weight in between 3000-3500 gms with respect to phototherapy given and not given. (i.e., $p<0.01$) (Fig. 2).

The equation for the least squares best fit line is, TSB = 3.185+0.724 (TCB), represented by the solid line (Fig. 3).

**Area under the curve:** The test result variable(s): CORDBILI has at least one tie between the positive actual state group and the negative actual state group. Statistics may be biased. The receiver operating characteristic (ROC) curve as shown above illustrates the discriminative performances of TcB indices and TSB levels at 72 hrs of age, to predict subsequent hyperbilirubinemia. The area under the ROC curve was 0.661 indicating a good predicted probability.

## DISCUSSIONS

The rural hospital affiliated with this medical college recorded a total of 4,350 neonatal births between July 2006 and June 2008, consisting of 4,276 live births and 74 stillborn infants. Among the 4,276 live births, there were 2,244 males and 1,877 females. The research study was conducted on a prospective cohort of 650 consecutive live newborns. Out of these 650 newborns, 377 (58%) were males and 273 (42%) were females.

Correlation Between Cord Bilirubin and 3rd Day TSB and TcB levels Karl Pearson's correlation coefficient indicated a positive relationship between cord bilirubin and TSB at 72 rs (+0.084) and between cord bilirubin and TcB at 72 hrs of age (+0.043).

**Predictive value of cord bilirubin (>2.5 mg $dL^{-1}$):** Cord bilirubin levels exceeding 2.5 mg $dL^{-1}$ demonstrated the ability to predict the development of significant hyperbilirubinemia, with a sensitivity of 78.18% and a negative predictive value of 86.66%.

**Cord bilirubin and serum bilirubin by weight groups:** In all three weight categories (2000-2500 g, 2501-3000 g and 3001-3500 g) the mean cord bilirubin levels were 2.76, 2.85 and 2.91 mg $dL^{-1}$, respectively, when serum bilirubin levels exceeded 13.5 mg $dL^{-1}$ at 72 hrs of age. Hence, cord bilirubin levels exceeding 2.5 mg $dL^{-1}$ can predict the occurrence of subsequent hyperbilirubinemia.

**Comparative studies on cord bilirubin:** Various studies, including those by Taksande *et al.*[13] Knudsen *et al.*[14] Jacobson *et al.*[16], Knüpfer *et al.*[5] and reported different predictive values of cord bilirubin levels in the development of neonatal jaundice[15-20].

**The role of cord bilirubin in abo-incompatibility:** Cord bilirubin levels, particularly in ABO-incompatible situations, indicate potential in utero hemolysis and a higher likelihood of subsequent hyperbilirubinemia.

**Correlation of 3rd day TSB and TCB:** Karl Pearson's formula revealed a correlation between 72-hrs TSB and TcB levels with a coefficient of +0.043, signifying a linear and statistically significant relationship. The least squares best fit line equation was TSB = 3.185+0.724(TCB).

**Validation of TcB measurement:** Studies by Vinod Bhutani *et al*.[18] and others demonstrated the reliability of TcB measurements and their correlation with the gold standard TSB measurements, making them useful in identifying infants at risk for clinically significant hyperbilirubinemia[14,20].

## CONCLUSION

**Demographic insights:** The rural hospital affiliated with the medical college in Pondicherry witnessed a significant number of neonatal births during the period of the study (between July 2006 and June 2008), with 4,350 recorded births. This highlights the need for effective neonatal care and healthcare services in the region.

**Gender distribution:** The data revealed a balanced gender distribution among the live-born neonates, with 2,244 males and 1,877 females. Understanding the gender distribution can assist in tailoring healthcare services to specific gender-related needs.

**Study cohort:** The study focused on a prospective cohort of 650 consecutively delivered live newborns. This cohort is a representative sample for the study's objectives and provides valuable insights into the health and well-being of these neonates.

**Gender composition of the cohort:** Within the study cohort, there was a slightly higher proportion of male neonates (377 or 58%) compared to female neonates (273-42%). This gender distribution within the cohort can be taken into consideration for gender-specific health interventions.

**Mode of delivery:** The majority of newborns in the study were delivered vaginally with vertex presentation (578-88.92%). However, there were also cases of cesarean section deliveries (72-11.08%). This information is essential for understanding the modes of delivery and their implications for neonatal health.

**Weight groups:** The study population was categorized into weight groups based on their g at birth, with 221 neonates (34%) in the 2000-2500 g group, 119 neonates (18.31%) in the 2501-3000 g group and 310 neonates (47.69%) in the 3001-3500 g group. This categorization is useful for assessing neonatal health outcomes in relation to birth weight.

**Hyperbilirubinemia and phototherapy:** A noteworthy finding was that 138 neonates (21.33%) experienced significant hyperbilirubinemia requiring phototherapy. This highlights the importance of having the necessary resources and expertise to manage and treat hyperbilirubinemia in neonates.

**Blood group incompatibility:** About 11.8% of the neonates had ABO blood group incompatibility with their mothers. This information is crucial for identifying neonates at risk and implementing appropriate interventions.

**Use of oxytocin for labor induction:** Oxytocin was administered for labor induction in 44 mothers (6.76%). This reflects common practices in obstetrics and can have implications for understanding labor management in the hospital.

**Predictive utility:** The correlation coefficient, as calculated by Karl Pearson, revealed a positive association between cord bilirubin and TSB at 72 hrs (+0.084) and between cord bilirubin and TcB at 72 hrs of age (+0.043).

Within the entire study cohort of 650 participants the relationship between paired values of Blil Check TcB and TSB was examined. The linear regression analysis demonstrated a significant correlation, represented by the equation TSB = 3.185+0.724(TcB). This signifies a positive correlation between cord bilirubin and TSB, as well as between cord bilirubin and TcB measurements, within the sample population of term infants, encompassing both sexes and birthweight categories and with no exclusion criteria related to hemolysis.

The Receiver Operating Characteristic (ROC) curve displayed an area under the curve of 0.661, indicating a favorable level of predictive accuracy.

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