

# Predictive Value of Transcutaneous Bilirubin Levels in Late Preterm Babies

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## ABSTRACT

**Introduction:** Neonatal hyperbilirubinemia is a frequent cause of readmission in hospital during the neonatal period. The present prospective analytical study was designed to evaluate the incidence, course and risk assessment of jaundice in late preterm infants.

**Material and methods:** Inborn late preterm infants (post menstrual age of 34 0/7 to 36 6/7 weeks) were observed for significant jaundice till 14 days of birth. Relevant antenatal, natal and postnatal histories were recorded prospectively in a pre-designed Performa. Each baby underwent transcutaneous bilirubin (TcB) measurement twice daily during the 1<sup>st</sup> 48 hours after birth. TcB measurements and perinatal risk factors were compared between babies who did or did not develop significant jaundice after 48 hours of birth.

**Result:** 247 late preterm babies were enrolled; out of which 59% developed significant jaundice. Mean gestation was 35.09 ± 0.86 weeks. Incidence of jaundice was higher in lower gestational age groups (p = 0.0078). Large for gestation age, ABO incompatibility and previous sibling with jaundice predicted significant hyperbilirubinemia. Pre-discharge TcB at 24-48 hours was a highly significant predictor variable and was better than clinical risk factors alone for prediction of significant subsequent jaundice.

**Conclusion:** Late preterm infants have a high incidence of significant jaundice. TcB measurements taken between 24-48 hours can significantly predict whether the baby would develop significant jaundice after 48 hours of life.

**Keywords:** Late preterm; Significant jaundice; Transcutaneous bilirubin

predictive of subsequent hyperbilirubinemia and readmission.<sup>5</sup> Several studies are available which have identified risk factors for significant post-discharge jaundice (i.e., requiring phototherapy or exchange transfusion as per hour-specific TSB nomogram of the AAP guidelines) but only a limited few are available which have evaluated the predictors in the late preterm infants. Hence the present study was conceptualized with the aim to evaluate the incidence, course and risk assessment of jaundice in late preterm infants.

## MATERIAL AND METHODS

The study was conducted in the post-natal ward at Rohilkhand Medical College and Hospital, Bareilly from November, 2014 to November 2016. All (289) consecutively born late preterm babies, intramural, whether delivered vaginally or by cesarean section, were included in the study. The eligibility criterion was post-menstrual age of 34 0/7 to 36 6/7 weeks. Exclusion criteria were Rh incompatibility, major congenital malformations and sepsis. Gestational age was determined by Modified Ballard's Score and mother's last menstrual period. Relevant antenatal, natal and postnatal histories were recorded prospectively in a pre-designed Performa. In each neonate, TcB measurement was taken twice daily (7 AM – 9 AM and 7 PM – 9 PM). The readings were taken from the forehead using transcutaneous bilirubinometer (Bilichek-HHU, Respironics). Whenever the neonate appeared jaundiced or when the TcB was > 12 mg/dL, TSB was performed. TSB was calculated from the capillary sample using spectrophotometer (Unibeam). The decision to treat jaundice was based on the TSB levels. Neonates with significant jaundice were started on phototherapy as per the AAP guidelines.<sup>4</sup> Infants with gestation 34 weeks and SGA infants were started on phototherapy at TSB levels 1mg/dL less than the treatment threshold on the AAP charts (this methodology was adopted from the study of Lavanya et al<sup>5</sup>). Babies discharged from the hospital were regularly followed in the outpatient clinic till day 14 of life or till appearance of significant jaundice. Study approval was taken from the Institute's Ethics Committee. Informed consent was taken from parents of every baby. Based on the hour of measurement, the TcB measurements were grouped into TcB 0-12 hours, TcB 13-24 hours, TcB 25-36 hours and TcB 37-48 hours. The clinical risk factors and the grouped

## INTRODUCTION

Neonatal hyperbilirubinemia affects nearly 84% of term newborns<sup>1</sup> and is the most common cause of hospital readmission during neonatal period.<sup>2</sup> Severe jaundice is rare (< 2%) but can lead to kernicterus and permanent neuro-developmental delay.<sup>2</sup> Neonatal hyperbilirubinemia is usually detected by the presence of icterus, but this approach can be quite unreliable especially in the first 24-48 hours when the total serum bilirubin (TSB) may be too low to be visualized consistently.<sup>3</sup> Transcutaneous bilirubinometry is becoming increasingly acceptable primarily because of convenience and non-invasive nature of its application. Modern day limitations have necessitated shortened stay in hospital for both mother and neonate, thereby reducing the time for hospital based professional assessment of infant feeding and detection of jaundice.<sup>4</sup> According to 2004 American Association of Pediatrics (AAP) clinical practice guidelines on the management of neonatal hyperbilirubinemia, 2004, combining of pre-discharge hour-specific nomogram measurements of total serum bilirubin (TSB) or transcutaneous bilirubinometry (TcB) along with risk factors such as lower gestational age and exclusive breast feeding are considered most

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TcB measurements were compared between infants with and without significant jaundice after 48 hours of life.

**STATISTICAL ANALYSIS**

SPSS version 21 was used for the analysis. Descriptive statistics and chi-square test were used to interpret results. Continuous variables were presented as mean ± SD and categorical variables as frequencies and percentages.

**RESULTS**

Two hundred eighty nine late preterm infants were born in the hospital during the study period, of which 247 were enrolled for the study. The male female ratio was 1.54:1. Two hundred and thirty four infants were followed till onset of significant jaundice or till day 14 of life (Figure-1). The mean gestation age was 35.09 ± 0.86 weeks and mean weight was 2289 ± 512 gms. Fifty four (23.07%), 79 (33.76%) and 101 (43.16%) neonates were of gestation ages 34, 35, and 36 weeks respectively. Twenty three (9.83%) neonates were small for age (SGA) and 18 (7.69%) were large for gestation age (LGA). Three (1.28%) infants were born of twin delivery. One hundred thirty nine neonates (59%) developed significant jaundice. The incidence of jaundice was highest at 34 weeks (68.52%), followed by 65.82% t 35 weeks and 49.5% at 36 weeks of gestation. (p = 0.0078). Mean duration of onset of significant jaundice was 54 ± 29 hours. Infants developing significant jaundice within first

24 hours were 1.21%; 29.96% infants between 25-48 hours and 25.1% infants after 48 hours of life.

The mean duration of phototherapy required was 52 ± 28 hours. The mean peak TSB was 14.8 mg/dL ± 2.8; 45% of the jaundiced infants had TSB > 15 mg/dL. In neonates who developed significant jaundice after 48 hours, the mean age of onset was 75 ± 26 hours, mean peak TSB was 14.6 ± 2.6 mg/dL and mean duration of phototherapy was 44 ± 21 hours.

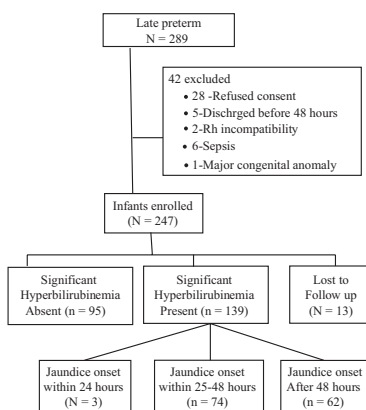
Following risk factors were seen to be significantly associated with neonates who developed significant jaundice: ABO incompatibility, lower gestational age (34 and 35 weeks), LGA, history of jaundice in previous sibling and birth trauma (Table-1). The median TcB values were 1.4 mg/dL, 3.8 mg/dL, 6 mg/dL and 7.7 mg/dL at 0-12 hours, 13-24 hours, 25-36 hours and 37-48 hours of life, respectively. The mean TcB values at 13-24 hours were significantly higher in infants developing significant jaundice between 24-48 hours as compared to those developing after 48 hours (4.8 ± 2.1 mg/dL vs. 4.0 ± 1.9 mg/dL (p = 0.0224).

Critical TcB levels, at 12-24 hours and 24-48 hours, of > 4.6 and > 7.4 mg/dL cut-off value respectively were selected based on sensitivity, specificity, positive predictive value and negative predictive value as shown in Table-2.

**DISCUSSION**

Hyperbilirubinemia is a common neonatal problem. Concern about neonatal hyperbilirubinemia is imperative, given the inherent risk of subsequent development of kernicterus. Newborns are physiologically predisposed to developing icterus and the risk is further compounded by prematurity. Over the years, several studies have been conducted to identify predictors of neonatal hyperbilirubinemia with the aim to limit unnecessary hospital stay and also to identify babies at risk for developing significant jaundice.

Out of the 234 late preterms enrolled for the study, 59% developed significant jaundice. This reiterates the fact that these infants need to be closely monitored for early recognition of jaundice. Similar incidence have been reported by other studies from India,<sup>6,7</sup> whereas another study conducted in term and near term infants reflected an incidence of 26%.<sup>8</sup> The higher



**Figure-1:** Enrollment and follow up of study subjects

Variable	Significant hyperbilirubinemia		p value
	Absent (n = 95)	Present (n = 62)	
Birth weight (gms)*	2349 ± 468	2368 ± 590	NS (p = 0.8230)
Gestation (wks)*	35.38 ± 0.69	35.22 ± 0.65	§
Males	50 (52.63)	35 (56.45)	NS (p = 0.6387)
SGA	6 (6.32)	8 (12.9)	NS (p = 1568)
LGA	4 (4.21)	12 (19.35)	HS (p = 0.0022)
ABO incompatibility	2 (2.11)	7 (11.29)	S (p = 0.0385)
Sibling jaundice	0 (0)	5 (8.06)	S (p = 0.0189)
Maternal oxytocin	4 (4.21)	6 (9.68)	NS (p = 2998)
Birth trauma	0 (0)	1 (1.61)	NS (p = 0.8292)
Exclusive breastfeeding	64 (67.37)	35 (56.45)	NS (p = 0.2293)
Stools/d**	2 (1-3)	2 (1-3)	NS (p = 0.9343)
Meconium passage (in d)**	2 (1-5)	2 (1-4)	NS (p = 0.9343)
TcB > 7.4 mg/dL at 24-48 hours (n=71)	13 (18.31)	58 (81.69)	ES (p < 0.0001)

\*Mean±SD; numbers in parenthesis are percentages; \*\* values in median (range); NS = not significant; S = significant (p < 0.01); HS = highly significant (p < 0.001); ES = extremely significant (p < 0.0001); § = p value between incidence at 34 wks and 36 wks; HS; p value between incidence at 35 wks and 36 wks; HS

**Table-1:** Risk Factors in Neonates With or Without Significant Jaundice Onset after 48 Hours

Variable	Sensitivity	Specificity	Positive predictive value	Negative predictive value
TcB level at 12-24 hours > 4.6 mg/dL	83.09%	87.37%	90.4%	78.3%
TcB levels at 24-48 hours > 7.4 mg/dL	93.55%	82.11%	81.69%	95.35%

**Table-2:** Sensitivity, specificity, positive predictive value and negative predictive values of TcB levels for prediction of hyperbilirubinemia

incidence in our study as compared to study by Sarici et al<sup>8</sup> may be due to inclusion of infants of 34 weeks gestation. Another retrospective study done on well babies showed that infants of gestation age  $\leq$  36 weeks, 36 1/7 weeks to 37 weeks, 37 1/7 weeks to 38 weeks had an odds ratio of 13.2, 7.7 and 7.2, respectively of developing significant jaundice as compared to babies > 40 weeks.<sup>5</sup> Similarly in our study, the incidence of developing significant jaundice was highest in babies of 34 to 35 weeks gestation as compared to babies of 36 weeks gestation ( $p = 0.0078$ ). The higher incidence of significant jaundice in late preterms is due to poor ligandin uptake of bilirubin by hepatocyte and decreased uridine diphosphate glucuronyl transferase (UDPGT 1A) activity in preterms.<sup>9,10</sup> Similar to other studies,<sup>10-12</sup> our study showed no significant relation between sex of the infant and development of significant hyperbilirubinemia. In contrast few researchers<sup>13,14</sup> reported male gender as a risk factor for jaundice.

In our study, assessment of pre-discharge risk factors showed that lower gestation age (34 and 35 weeks), large for gestation age (LGA), ABO incompatibility and previous sibling with jaundice were the clinical variables that were significantly associated with significant hyperbilirubinemia. Similar findings have been reported earlier.<sup>6,7,15,16</sup>

Pre-discharge TcB at 24-48 hours was a highly significant predictor variable and was better than clinical risk factors alone for prediction of significant subsequent jaundice. Negative predictive value of 95.35% shows that measurement of TcB at 24-48 hours can very efficiently predict the risk of subsequent jaundice. Similar observations were reported by Lavanya et al.<sup>6</sup> In a prospective cohort study, Keren et al found that combining pre-discharge TcB measurements along with gestational age improved the accuracy of prediction of subsequent jaundice.<sup>17</sup> Since more than 50% of late preterm babies are at risk of developing significant jaundice, pre-discharge TcB levels should be routinely performed to decide which babies require delayed discharge or early follow-up for neonatal hyperbilirubinemia.<sup>18</sup>

## CONCLUSION

Late preterm infants have a high incidence of significant jaundice. TcB measurements taken between 24-48 hours can significantly predict whether the baby would develop significant jaundice after 48 hours of life.

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