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The role of first day serum bilirubin estimation in predicting significant hyperbilirubinemia in healthy term newborns

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ABSTRACT

Introduction: Neonatal hyperbilirubinemia remains a public health concern as documented by recent reports of kernicterus in otherwise healthy term and near term newborns. Kernicterus in such newborns is preventable, provided excessive hyperbilirubinemia for age is promptly identified and appropriately treated

Objectives: 1) To determine the predictive ability of 6thhr and 24thhr Total serum bilirubin (TSB) values for subsequent significant hyperbilirubinemia in healthy term newborns. 2) To establish cut off values and comparison of obtained value for predicting significant hyperbilirubinemia. 3) To predict the risk of jaundice, in order to implement early treatment and there by minimize the risk of bilirubin dependent brain damage.

Methods: This study was a hospital based prospective study to determine predictive ability of hour specific bilirubin (at 6thhr and 24thhr) for subsequent hyperbilirubinemia in healthy term neonates. Blood samples on 6th and 24th hr were taken for bilirubin estimation and followed up to 72ndhr for significant hyperbilirubinemia.

Results: 7 out of 34 healthy term newborns with 6thhr TSB of ≥2 mg/dl developed significant hyperbilirubinemia in comparison to 6 out of 216 newborns with 6thhr TSB of <2mg/dl and this arbitrary cut off value of 2mg/dl is statistically significant. 80.8% of newborns had 24 hr TSB of <5mg/dl and 19.2% had ≥ 5 mg/dl and the cut off value of 5.0mg% can predict subsequent significant hyperbilirubinemia with sensitivity of 100% and specificity of 85.2%.

Conclusion: A screening TSB should be done for every newborn at the earliest, in order to predict those at risk for subsequent hyperbilirubinemia and allow for a safer discharge.

Key words: ***Hyperbilirubinemia, Kernicterus, Neonatal, Total serum bilirubin***

Introduction

Hyperbilirubinemia is a universal presentation in the newborn period and is recognized as clinical jaundice in approximately 50% of infants. Neonatal hyperbilirubinemia remains a public health concern as documented by recent reports of kernicterus in otherwise healthy term and near term newborns. Kernicterus in such newborns is preventable, provided excessive hyperbilirubinemia for age is promptly identified and appropriately treated [1,2].

With an intent to facilitate such identification and treatment, universal screening for severity of hyperbilirubinemia before hospital discharge may predict that extraordinary segment of the neonatal population that are at risk for excessive hyperbilirubinemia during the first week after birth [3].Under normal circumstances, the level of indirect reacting bilirubin in umbilical cord serum is 1-3mg/dl and rises at a rate of less than 5mg/dl/24hrs. Thus jaundice becomes visible on the 2nd or 3rd day (36-72hrs) with the indirect reacting bilirubin usually reaching peak value of 5-

6mg/dl by the 3rd day and decreasing to below 2mg/dl between 5th and7th day of life [4].

Early discharge of healthy term newborns after delivery has become a common practice in our country because of medical and social reasons as well as economic constraints [5,6]. In significant number (6.5%) of babies, hyperbilirubinemia is the most common cause for readmission during the early neonatal period [7].

In up to 4% of term newborns who are readmitted to the hospital during their first week of life, approximately 85% are readmitted for jaundice [8]. While jaundice per se is not preventable, early detection of threatening bilirubin levels permit initiation of phototherapy and prevents higher risk and high cost exchange transfusion therapy or kernicterus. The concept of prediction of jaundice offers an attractive option to pick up babies at risk for neonatal hyperbilirubinemia. An association between bilirubin levels and subsequent risk of hyperbilirubinemia has been reported [9,10].

Several investigators have tried to find a simple marker to predict hyperbilirubinemia in newborns. Some of them used cord bilirubin estimation [11-19], bilirubin estimation during 6 to 24 hours of age [20-23], pre-discharge hour specific bilirubin estimation [24], Transcutaneous bilirubin measurement [25,26] and ETCO (End Tidal Carbon Monoxide) measurement [27,28] to predict the subsequent course of Jaundice. The gold standard for deciding therapy to prevent encephalopathy continues to be serum bilirubin levels for want of better parameters. Hour specific percentile charts based on serum bilirubin at different postnatal ages have been developed[29]. They show that subsequent hyperbilirubinemia can be predicted with reasonable accuracy by plotting for specific bilirubin on these charts. There is paucity of literature on this concept of prediction of hyperbilirubinemia. The present study was carried out to evaluate the predictive value of specific bilirubin level with in 24 hrs of postnatal age for identifying term neonates at risk for subsequent hyperbilirubinemia.

Materials & Methods

I. Study design

This study was a hospital based prospective study to determine predictive ability of hour specific bilirubin (at 6thhr and 24th hr.) for subsequent hyperbilirubinemia in healthy term neonates.

II. Sample size

Total of 250 healthy term newborns delivered at S.V.R.R. Govt. Maternity hospital, Tirupati were included with birth weight ≥ 2500 grams and gestational age ≥37 wks.

III. Setting

The study, approved by ethical committee on 25th December 2011, was undertaken in the postnatal care ward at S.V.R.R.Govt. Maternity Hospital, Tirupati with neonatal unit attached to it.

IV. Period of study

The study covered a period of one year from March 2012 to February, 2013.

V. Selection of study subjects

The study subjects have been selected based on systematic random sampling Technique by using $4PQ/I^2$ formula. A sample size of 280 has been selected for the present study, taking exclusion criteria into consideration. First baby was selected based on computer generated Random number table. Based on systematic Random sampling, every 30th baby which meets inclusion criteria has been selected as study subjects. During the study, 30 babies have been excluded from the study due to conjugated hyperbilirubinemia, NICU admission and incomplete data. So, a total of 250 babies have been enrolled for the study.

Inclusion Criteria

Healthy term babies with birth weight ≥ 2500 grams and gestational age ≥37 wks born at SVRR GMH, Tirupati.

Exclusion Criteria

1. Preterm<37 wks and post term>42 wks
2. Babies with significant illness requiring NICU admission
3. Rh incompatibility
4. ABO incompatibility
5. IUGR babies
6. Babies with major congenital malformations
7. Babies with conjugated hyperbilirubinemia
8. Babies with APGAR<5 at 5 min
9. History of intake of drugs in mothers affecting fetal liver eg: sulphonamides, nitrofurantoin, anti-malarial.
10. Those that did not stay till 72 hrs of life

VI. Ethical issues

Informed consent was taken from parents before enrolling the babies for study.

VII. Methodology

The Study group was evaluated by a designed protocol. In all newborns detailed history, gestational assessment by Expanded Ballard score, systemic general examination with particular attention to the factors known to be associated with hyperbilirubinemia was carried out. Blood samples on 6th and 24th hr were taken for bilirubin estimation.

VIII. Laboratory evaluation (Bilirubin estimation)

Serum bilirubin estimation was done using *Malloy and Evelyn* method.

VIII. Statistical Analysis

Maternal and neonatal data were collected using predesigned and pretested proforma. The results for each parameter were presented in Tables and charts. Bilirubin values were plotted on previously published nomogram. Data analysis was carried out using MS excel, Epi info, 3.5.1 version. For determining significance of each test p value was used. Sensitivity, specificity, positive predictive value, negative predictive value and likelihood ratio of the test were calculated.

Results

A total of 280 healthy term newborns were evaluated. Of these, 30 babies were excluded from study as 3 babies had conjugated hyperbilirubinemia, 12 babies had NICU admission after 24 hrs and 15 babies had incomplete data. So, a total of 250 babies were enrolled for study. 6th hour and 24 hour of life TSB levels were obtained.

Majority (49.2%) of newborns had 6th hour TSB level between 1-1.4 mg/dl. Only 34 newborns out of 250 had 6th hour TSB level > 2mg/dl (Table: 1).

When the values of TSB are analyzed gestational age-wise groups (Table.2) in the 37-38 Wks gestational age category 42.2% of newborns had 6th hour TSB levels between 1-1.4 mg/dl followed by 38.7% I with TSB levels of 1.5-1.9 mg/dl. 21 and 14.7% newborns of TSB levels between 2-2.4 mg/dl among 37-38 Wks gestational age category. Only 2 (1.4%) newborns had 6th hour TSB levels >2.5 mg/dl among 37-38 Wks gestational age category.

In the 39-40 wks gestational age group also 55.4% of newborns had 6th hour TSB levels between 1-1.4 mg/dl, 8.4%are between 2-2.4 mg/dl and only 1 newborn had 6th hour TSB levels >2.5 mg/dl among 39-40 Wks gestational age category (Table.2).

In the 41-42 wks gestational age category 64% newborns had 6th hour TSB levels between 1-1.4 mg/dl followed by 16% in 1.5-1.9 mg/dl, 12% in 2-2.5mg/dl and 8% in 0.5-09 mg/dl groups and no baby had 6th hour TSB level > 2.5 mg/dl (Table: 2).

The bilirubin values at 24th hour in the newborns were in the range of 1.4-8.8 mg/dl. In the present study 80.8% (202/250) of newborns had their 24th hr TSB level ≤ 4.9 mg/dl corresponding to the *low risk zone*. 18% (45/250) newborns had their 24th hr TSB level between 5.0-7.9 mg/dl corresponding to *intermediate risk zone.* Only 3 (1.2%) newborns had 24th hr TSB level between 8.0-8.9 mg/dl corresponding to *high risk zone* (Table: 3.).

Table: 1. Distribution of study population according to 6th hour TSB levels

6thhr. TSB level(mg/dL)	Number	Percentage
0.5 – 0.9	7	2.8
1 – 1.4	123	49.2
1.5 – 1.9	86	34.4
2 – 2.5	31	12.4
> 2.5	3	1.2

Table: 2. 6th hour TSB distribution according to gestational age

6thhr TSB(mg/dL)	37-38 Wks	39-40Wks	41-42 Wks
0.5 – 0.9	4 (2.9%)	2 (2.5%)	2 (8%)
1 – 1.4	60 (42.2%)	46(55.4%)	16 (64%)
1.5 – 1.9	55(38.7%)	27(32.5%)	4 (16%)
2 – 2.5	21 (14.8%)	7(8.4%)	3 (12%)
> 2.5	2(1.4%)	1(1.2%)	0
Total	**142**	**83**	**25**

X^2=6.33: p=0.04; S

Table: 3. Distribution of study population according to 24th hour TSB levels

24 hr TSB level(mg/dL)	Number	Percentage
1-1.9	5	2
2-2.9	38	15.2
3-3.9	78	31.2
4-4.9	81	32.4
5-5.9	32	12.8
6-6.9	12	4.8
7-7.9	1	0.4
8-8.9	3	1.2
Total	**250**	**100**

When the values of TSB are analyzed gestational age-wise groups (Table: 4) 83.3% (115/142) of newborns among 37-38 Wks of gestational age had 24 hour serum bilirubin level in the *low risk zone* (≤ 4.9 mg/dl) followed by 18.3% (26/142) in the *Intermediate risk zone* (5.0-7.9 mg/dl) and only one case (0.7%) in the *High risk zone* (≥ 8.0 mg/dl).

In the 39-40 wks gestational age group also 83.13% (69/83) of newborns had 24th hour TSB levels in the (Table.4) *low risk zone* (≤ 4.9 mg/dl) followed by 14.45% (12/83) in the *Intermediate risk zone* (5.0-7.9 mg/dl). And only 2 (2.4%) newborns in the *High risk zone* (≥ 8.0 mg/dl).

In the 41-42 wks gestational age group also 72% (18/25) of newborns had 24th hour TSB levels in the (Table: 4) *low risk zone* (≤ 4.9 mg/dl) followed by 28% (7/25) in the *Intermediate risk zone* (5.0-7.9 mg/dl). No newborns in the *High risk zone* (≥ 8.0 mg/dl) were observed in this group.

As per the Bhutani nomogram[24] out of 250 cases of newborn 202 (80.8%) fell in the low risk zone, 45(18%) in intermediate risk zone and 3 (1.2%) in high risk zone (Table: 5)

When the data was analyzed for subsequent risk of developing hyperbilirubinemia (Table: 6) a total of 13 newborns developed significant hyperbilirubinemia. Newborns who developed significant hyperbilirubinemia were subjected to phototherapy. No newborn belonging to low risk zone developed significant hyperbilirubinemia. 33.33% (15/45**)** of newborns in the intermediate risk zone remained in *low risk* zone. 17.77% (8/45) newborns in the intermediate risk zone went up to *low-intermediate risk* zone. 26.66% (12/45) newborns in the intermediate risk zone went up to *high-intermediate risk* zone. 22.22% (10/45) newborns in the intermediate risk zone went into *high risk* zone. All the 3 newborns belonging to high risk zone remained in

high risk zone. Among 250 newborns, 237 (94.8%) did not develop significant hyperbilirubinemia and 13(5.2%) developed significant hyperbilirubinemia.

On detailed analysis of those with significant hyperbilirubinemia (Table: 7) 7/13 newborns had 6th hr TSB level ≥ 2.0 mg/dl.and5/13 newborns had 6th hr TSB level between 1.0 - 1.8 mg/dl. Only *one baby* had 6th hr TSB level < 1.0 mg/dl.10/13 newborns had their 24 hour TSB level in Intermediate zone. 3/13 newborns had their 24 hr TSB level in High risk zone. Maximum number of newborns (80.8%) had their 24 hr TSB levels <5 mg/dl, that correspond to low risk zone of Bhutani's nomogram. In the present study only 48/250 (19.2%) had 24 hr TSB levels >5 mg/dl.

Six newborns among 216 with 6th hr TSB of <2 mg/dl had significant hyperbilirubinemia. Seven newborns out of 34 with 6th hr TSB of ≥2 mg/dl had significant hyperbilirubinemia. The predictive ability of cut off level of 2 mg% is as follows: Specificity: 88.6%, Sensitivity: 53.8%%,

Positive predictive value: 20.6%, Negative predictive value: 97.2%, $\chi 2$ =18.8, P value : < 0.001 *(significant)* and Kappa value=0.24 (fair agreement).

No newborn with 24hr TSB of <5mg/dl had significant hyperbilirubinemia. 13 out of 48 newborns with 24 hr TSB of ≥5mg/dl had significant hyperbilirubinemia. The predictive ability of cut off level of 5 mg% for Table: 8 is as follows:-

Specificity: 85.2%, Sensitivity: 100%, Positive predictive value: 27.1%, Negative predictive value: 100%, $\chi 2$ =57.7%, P value : < 0.001 *(significant) Kappa* value=0.24 (fair agreement).

Table 4: Distribution of TSB levels at 24th hour according to gestational age

24 hr TSB(mg/dL)	37-38 Wks	39-40Wks	41-42 Wks
1-1.9	2	1	2
2-2.9	24	9	5
3-3.9	41	32	5
4-4.9	48	27	6
5-5.9	19	9	4
6-6.9	6	3	3
7-7.9	1	0	0
8-8.9	1	2	0
Total	**142**	**83**	**25**

Table: 5. Risk stratification of study population based on 24th hour TSB levels

Bhutani et al[24] (risk zone)	Number of newborns	Percentage
Low risk(<40th centile)	202	80.8
Intermediate risk (40-95th centile)	45	18
High risk > 95th centile	3	1.2
Total	**250**	**100**

Table: 6. Subsequent risk categorization of study population at 72hrs

24 hr TSB		Subsequent risk categorization of study population at 72 hrs			
Risk zone	**Number of Newborns**	**Low Risk**	**Low intermediate risk**	**High intermediate risk**	**High Risk**
Low risk zone (<40th centile)	202	191	11	0	0
Intermediate risk zone (40-95th centile)	45	15	8	12	10
High risk zone (>95th centile)	3	0	0	0	3
Total	**250**	**206**	**19**	**12**	**13**

X^2=130.4: p<0.001;

Table: 7. Risk stratification in newborns with significant hyperbilirubinemia

S.No	TSB at 6th hr in mg/dl	TSB at 24 hr in mg/dl	Risk Zone	TSB at 72 hr in mg/dl
1	1	5	Intermediate	17.6
2	0.8	7.2	Intermediate	17.2
3	1	6.7	Intermediate	17.9
4	1.2	5.5	Intermediate	19.2
5	2	6.5	Intermediate	18.2
6	2	6	Intermediate	18.4
7	1.8	8.8	High	17.5
8	2.1	6.8	Intermediate	17
9	2.3	8.7	High	19.3
10	2.1	8.8	High	19
11	2.8	6.8	Intermediate	17
12	1.7	5	Intermediate	20
13	2.2	5.3	Intermediate	18.1

Discussion

Recent case reports and experience of neonatologists suggest the possible re-emergence of kernicterus from a state of near extinction to one that is of concern to pediatricians[30]. The re-emergence of kernicterus is the result of interacting phenomena including a) early hospital discharge (before extent of jaundice is known and signs of impending brain damage have appeared); b) lack of adequate concern for the risk of severe jaundice in healthy term and near term newborns; c) medical care cost constraints leading to early discharge with loss of supervision; d) paucity of educational materials to enable parents to participate in safeguarding their newborns; and e) limitations within the health care systems to provide continuity of care.

Whatever are the demographic risk factors, one thing is certain, if babies leave the hospital before they are 36 hours old, their peak bilirubin level will occur after they are discharged. Thus, jaundice today is largely an outpatient problem and if we want to ensure that we do not miss the occasional baby who develops a very high bilirubin level, we need to reconsider our approach.

Pre-discharge Jaundice as predictor vector for subsequent hyperbilirubinemia

Quantifying the level of jaundice has been the foundation for satisfactory management of hyperbilirubinemia. Early visual recognition of jaundice and accurate estimation of its severity is crucial for effective implementation of the AAP guidelines.

Serum bilirubin levels are usually 1-3 mg/dl at birth and rise at a rate of less than 5 mg/dl per day peaking at 2-3 days in term and 5-7 days in preterm. It should be remembered that bilirubin rises by the hours of life and hence the time of sampling must be as ‘hours of life’ and not ‘day of life’.

Our study hypothesis was that a high serum bilirubin level soon after birth would also predict a high peak later in life. 250 normal healthy term newborns were evaluated in S.V.R.R and Govt maternity hospital, Tirupati for neonatal hyperbilirubinemia using 6thhr TSB level and total serum bilirubin (TSB) level at 24th hour as predictor. We have considered peak Serum bilirubin level > 15 mg/dl as ‘Significant hyperbilirubinemia’ since specific treatment is usually considered at or above this level [31].

Estimation of TSB at 6 hrs

In a study done by Sarici et al[32] 6thhr TSB was done in term and late preterm newborns and repeated daily for 4 days. Comparison was made between two groups. 10.5% in the Term group and 25.3% in the late preterm group had significant hyperbilirubinemia.

In the Present study, only healthy term newborns were studied and 7 out of 34 newborns with 6th hr TSB of ≥2 mg/dl developed significant hyperbilirubinemia in comparison to 6 out of 216 newborns with 6th hr TSB of <2mg/dl and this arbitrary cut off value of 2mg/dl is statistically significant.

Estimation of TSB at 24 hrs

Bhutani[33,34] and co-workers obtained serum bilirubin levels between 20-28 hours of age in 1097 newborns. None of them who had bilirubin level of less than 5 mg/dl at 24 hours developed a serum bilirubin level of more than or equal to 17 mg/dl; whereas 33% of those whose 24 hours serum bilirubin level was at least 8 mg/dl developed a serum bilirubin level of at least 17 mg/dl.

Seidman et al[35] used a similar approach in Israeli newborns and found that the risk of bilirubin level of at least 17 mg/dl was 1.6% in those whose bilirubin levels were less than 5 mg/dl at 24 hours versus 6.6% of those whose bilirubin levels were at least 5 mg/dl at 24 hours.

In the study done by Agarwal et al[22], TSB was estimated at 24 ± 6 hours. In another Indian study done by Awasthi et al [20] TSB level was estimated at 18-24 hours. In the present study the range of bilirubin value was from 1.4 mg/dl to 8.8 mg/dl, average bilirubin value being 4.06 mg/dl. In the study done by Awasthi et al, the average bilirubin level was found to be 3.99 mg/dl.

Evaluation of bilirubin value to predict Neonatal Hyperbilirubinemia using available protocols

Depending on the TSB at 24 hours we divided our newborns in two groups using arbitrary cut off value of 5.0mg%. 80.8% of newborns had 24 hr TSB of <5mg/dl and 19.2% had ≥ 5 mg/dl. When newborns were classified into two groups using cut off value of 5 mg%, no newborn that had bilirubin < 5 mg% developed significant hyperbilirubinemia requiring phototherapy. Out of 48 newborns that had their first bilirubin level ≥ 5 mg%, 13 developed

significant hyperbilirubinemia requiring phototherapy. Thus the cut off value of 5.0mg% can predict subsequent significant hyperbilirubinemia with sensitivity of 100% and specificity of 85.2%.

P value is less than 0.001 indicating the significance

Alpay et al[21] reported that TSB level ≥ 6.0 mg/dl in the first 24 hours of life will predict nearly all of the term newborns who will have significant hyperbilirubinemia and will determine all those who will require phototherapy treatment later during the first days of life (Table: 9).

Agarwal et al[22] did one study to evaluate predictive value of TSB level 6.0 mg % at 24 ± 6 hours postnatal age in identifying near term and term newborns that do not develop hyperbilirubinemia subsequently. In their study first bilirubin estimation was done at 24 ± 6 hours. Subsequent bilirubin estimation was done whenever clinical suspicion of jaundice exceeded 10.0 mg%. Out of 213 newborns studied, 22 developed significant hyperbilirubinemia requiring phototherapy. TSB level of 6 mg/dl or less was present in 136 (63.8%) newborns and only one developed hyperbilirubinemia. In the remaining 77 (36.2%) neonates with TSB > 6 mg/dl hyperbilirubinemia developed in 21 (sensitivity 95%, specificity 70.6%).

Alpay et al[21] and Agarwal et al[22] concluded that ideal cut off value was 5.0 mg/dl and babies with TSB levels higher than 6.0 mg% had a significant risk of developing hyperbilirubinemia. In the study done by Awasthi et al[20], a value of 3.99 mg/dl (average value of first day TSB) was used to predict occurrence of subsequent hyperbilirubinemia. The sensitivity and specificity of this test was 67%. However this study had major flaws. Complete follow up was present in newborns who stayed in the hospital either for neonatal illness or some maternal reason, such as caesarean section. More than 50% of newborns, who were healthy thus discharged early, were not followed up for risk stratification.

Bhutani et al[24] did a study to assess the predictive ability of universal pre discharge serum bilirubin measurement to screen for the risk of subsequent significant hyperbilirubinemia in direct coomb's negative healthy term / near term newborns during first postnatal week. TSB was obtained at the time of routine metabolic screening in all term / near term newborns. A percentile based nomogram for the first week was constructed from hour specific pre discharge and post discharge TSB values of newborn. The nomogram has 3 risk zones[24]

Low risk zone < 40th centile.

Intermediate risk zone

Low intermediate 40th – 75th centile.

High intermediate 75th – 95th centile.

High risk zone > 95th centile.

When newborns in our study were divided in 3 risk zones using nomogram prepared by Bhutani et al[33,34], and compared with that of Bhutani et.al and Umesh Pathak et al[36] (Table: 10) the percentage of newborns in high risk zone i.e. bilirubin value more than 95th centile were less in the present study. Similarly those in the in intermediate risk zone i.e. bilirubin value between 40th – 95th centile was also less in the present study. In the low risk zone i.e. bilirubin value less than 40th centile the percentage is more in the present study when compared to that reported in literature by Bhutani et.al and Umesh Pathak et.al., The low risk zone of this nomogram corresponds to the arbitrary cut off bilirubin value. Subsequent bilirubin estimation was done at 72 hrs

On subsequent follow up

Of the 80.8% (202/250) newborns in low risk zone 191 (94.5%) newborns remained in low risk zone subsequently. 11 (5.4%) newborns went up to low intermediate risk zone. No newborn went up to high intermediate risk zone. No newborn went into high risk zone. No newborn, thus belonging to low risk zone developed significant hyperbilirubinemia requiring phototherapy.

Of 18% (45/250) newborns in intermediate risk zone 10 (22.22%) newborns went into high risk zone, developed significant hyperbilirubinemia requiring phototherapy and 8 (17.77%) newborns moved down to low intermediate risk zone.15 (33.33%) newborns moved down to low risk zone.12 (26.66%) newborns went up to high intermediate risk zone.

Of 1.2 % (3/250) newborns in high risk zone, all 3 (100%) newborns remained in high risk zone, developed significant hyperbilirubinemia and required phototherapy.

In the study done by Bhutani et al[24], pre discharge 6.1 % of the study population was in high risk zone, of these 39.5 % remained in this zone. Pre discharge 32.1 % population had TSB values in

the intermediate risk zone. In a clinically significant minority of these newborns, the post discharge TSB moved into the high risk zone. The pre discharge TSB in 61.8 % newborns was in low risk zone and there was no measurable risk for significant hyperbilirubinemia. The authors concluded that an hour specific TSB before discharge can predict which newborn is at high / intermediate / low risk for developing clinically significant hyperbilirubinemia.

Outcome: Total of 13 newborns out of 250 developed significant hyperbilirubinemia requiring phototherapy. 11 newborns had their 24 hr TSB level more than 5.0 mg/dl. Only 2 newborns had 24 hr TSB equal to 5.0 mg/dl. 3 of these 13 newborns had their 24 hr TSB value in high risk zone, 10 newborns had their 24 hr TSB value in intermediate risk zone and none had 24 hr TSB value in low risk zone.

Predictive value: In each test negative predictive value (NPV) is more significant than positive predictive value (PPV). If a newborn becomes hyperbilirubinemic, the probability that TSB at 24 hrs was ≥ 5mg/dl was 100% (sensitivity).The probability that TSB at 24 hrs was<5mg/dl was 85.2% (specificity) in a newborn without hyperbilirubinemia (Table.12). Newborns with bilirubin less than the cut off value or bilirubin level in low risk zone can be discharged safely and early. It also highlights that the risk stratification is an excellent method of tracking newborns with hyperbilirubinemia as newborns with hour specific bilirubin value in low risk zone have no risk of developing subsequent significant hyperbilirubinemia.

Table: 8. Predictive characteristics of percentile tracts as risk demarcators for subsequent significant hyperbilirubinemia according to Bhutani'snomogram

Location of predictive bilirubin value at 24 hrs		Outcome : Subsequent hyperbilirubinemia		Predictive characteristics (%)				
Percentile track as risk demarcators	No. of newborn	Present	Absent	PPV	NPV	Sensitivity	Specificity	Kappa statistic
Above 95th percentile	3	3	0	100	95.9	23	100	0.36 (Fair agreement)
Below 95th percentile	247	10	237					
Above 75th percentile	16	11	5	68.8	99.1	84.6	97.9	0.74 (Substantial Agreement)
Below 75th percentile	234	2	232					
Above 40th percentile	48	13	35	27.1	100	100	85.2	0.38 (Fair agreement)
Below 40th percentile	202	0	202					

Table: 9. Comparison of predictive value of TSB

Study	Arbitrary cut off TSB value	Neonates with hyperbilirubinemia above cutoff value	Neonates with hyperbilirubinemia below cutoff value	Sensitivity	Specificity
Agarwal et al [22]	6.0 mg/dl	21/77(27.2%)	1/136(<1%)	95%	70.6%
Alpay et al [21]	6.0 mg/dl	54/206 (26.21%)	6/292(2.05%)	90%	85%
Present study	5.0 mg/dl	13/48(27.08%)	0/202(0%)	**100%**	**85.2%**

Table: 10. Risk Stratification of the Study Population

Risk zone	Bhutani et al[24]		Umesh Pathak et al[36]		Present study	
	No.	%	No.	%	No.	%
High risk	172	6.1	49	5.3	3	1.2
Intermediate risk	912	32.1	537	42.1	45	18
Low risk	1756	61.8	342	36.8	202	80.8
Total	**2840**	**100**	**928**	**100**	**250**	**100**

Table: 11. Predictive characteristics for subsequent significant hyperbilirubinemia

Study	Risk zone	PPV (%)	NPV (%)	Specificity (%)	Sensitivity (%)
Umesh Pathak et al[36]	High risk zone	69.4	81.2	97.9	17.1
	Low risk zone	28.5	90.6	42.5	83.9
Present study	High risk zone	100	95.9	100	23
	Low risk zone	27.1	85.2	85.2	100

Table 12: Comparing the various protocols following results were obtained

Test	Sensitivity	Specificity	Positive Predictive value	Negative predictive value
Using arbitrary cut off 5 mg/dl	**100**	**85.2**	**27.1**	**100**
Risk stratification (Low risk zone)	**100**	**85.2**	**27.1**	**100**

Conclusion

- In the present study,13(5.2%) out of 250 newborns, developed significant Hyperbilirubinemia and 37-38 wks (84.6%) was the most common gestational age group associated with significant hyperbilirubinemia.
- 6thhr TSB cut off value of 2 mg/dl has good specificity and is statistically significant in predicting newborns with subsequent significant hyperbilirubinemia.
- Hour specific bilirubin level i.e. total serum bilirubin (TSB) of less than 5.0 mg% at 24 hrs predicts absence of subsequent hyperbilirubinemia with high probability. Term neonates whose first bilirubin level is above the cut off value of 5.0 mg/dl are more prone to develop significant hyperbilirubinemia requiring phototherapy.
- Neonates in Low risk zone (100%) are at the least risk, hence can be discharged safely & early.
- Neonates in Intermediate risk zone (22.22%) are the most vulnerable for developing hyperbilirubinemia, requiring intensive monitoring & watchful evaluation to prevent significant morbidity.
- Neonates in High risk zone (100%) require appropriate intervention at the earliest to prevent BIND & kernicterus**.**
- Hour specific percentile curves have good predictive ability for subsequent hyperbilirubinemia.
- A screening for TSB should be done for every newborn at the earliest, in order to predict those at risk for subsequent hyperbilirubinemia and allow for a safer discharge.

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