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Original Research Article

Evaluation of the Diagnostic Accuracy of Non-Invasive Hand Held Transcutaneous Bilirubinometer for the Diagnosis of Neonates with Hyperbilirubinemia

Rupesh Kumar[1], Juli[2], Akhilesh Kumar[3]

[1]Senior Consultant, Department of Neonatology, Yashvi Children Hospital, Patna, Bihar, India
[2]Senior Resident, Department of Pathology, Bhagwan Mahavir Institute of Medical Sciences, Pawapuri, Nalanda, Bihar, India
[3]Assistant Professor, Department of Microbiology, RDJM Medical College and Hospital, Turki, Muzaffarpur, Bihar, India

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Corresponding author: Dr. Juli
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Abstract:

Aim: The aim of the present study was to assess the diagnostic accuracy of TCB compared with the total serum bilirubin (TSB) measurement in infants more than and equal to 35 weeks at different sites during the neonatal period and implementation of the results for better management of jaundiced neonates

Material & Methods: This is a prospective, observational, cross sectional, hospital-based study done on newborn babies between 350/7 weeks to 416/7 weeks of gestation for the duration of 12 months at Department of Pathology and Neonatology. 200 neonates were included in the study.

Results: The mean birth weight of the sample is 2992 gm (95% CI-2906.39-2986.01) with a standard deviation of 390.7 gm. The neonate with minimum weight in the study population was of 2505 gm and maximum of 4000 gm. Mean transcutaneous bilirubin level measured at forehead is 12.38 mg/dl (95% confidence Interval-12.02-12.66) with a SD of 3.16 mg/dl. Mean transcutaneous bilirubin level measured at sternum is 12.32 mg/dl (95% confidence Interval-11.97-12.71) with a SD of 3.14 mg/dl. Mean serum bilirubin level is 12.98 mg/dl (95% confidence Interval-11.6-12.32) with a SD of 3.57 mg/dl. The correlation between the readings of serum and transcutaneous bilirubinometer <15 mg/dl is very high at forehead (r=0.96, p=0.001) and sternum (r=0.92, p=0.001). Our observation on visual assessment of jaundiced neonates 4% fall in Kramer's stage 1, about 14% are found in Kramer stage 2, In stage 3 highest percentage 30% (n=60) of neonates are falling in, 25% (n=50) found in stage 4 and in a stage 5. 27% (n=54) neonates are seen. The sensitivity of TCB at sternum remains 100% at low risk zone as well as at high risk zone, when measured at >120-168 hrs of life.

Conclusion: The findings of the present study indicate that the TCB is a reliable screening tool for hyperbilirubinemia in newborns >35 weeks of gestation, especially with bilirubin levels ≤15 mg/dl in 2-7 days of life. TCB can be a viable option for universal screening. Incorporating the use of TCB devices in clinical practice, can reduce the need for blood sampling for the management of neonatal jaundice.

Keywords: Neonatal jaundice, Transcutaneous bilirubinometer, Serum bilirubin, Kernicterus.

Introduction

Newborns typically exhibit elevated bilirubin levels during their initial days of life, a condition known as Physiological Jaundice. Neonatal jaundice is a common condition that frequently presents in 1–2 wk old neonates, and is one of the most common causes of hospital admission of young infants, especially in Asia. [1] Neonatal Jaundice impacts a significant portion of the neonatal cohort, affecting approximately 60% of full-term infants and 80% of preterm infants. [2,3] However, this physiological jaundice can be exacerbated or prolonged due to various factors. Unconjugated (indirect) hyperbilirubinemia represents a prevalent and generally benign condition frequently observed in neonates. Jaundice (icterus neonatorum), manifests through noticeable effects on various bodily tissues. One of the prominent indicators is the impact it has on the skin, sclera (the white part of the eyes), and mucous membranes. This condition results from a metabolic imbalance where bilirubin synthesis surpasses hepatic-enteric bilirubin clearence. The immaturity of the neonate's blood-brain barrier renders it permeable to a substantial bilirubin influx into the brain, thereby posing the potential risk of inducing a spectrum of irreversible cerebral injuries. [3]

The mortality rate of neonatal jaundice can be reduced by instant diagnosis and appropriate treatment. Although intensity and localization of jaundice is commonly used as an indicator of bilirubin blood concentration, the correlation between visual estimation and actual bilirubin concentration is poor. [4,5] At present, total serum bilirubin (TSB) is the gold standard for diagnosing neonatal jaundice. Two methods can be used to estimate TSB, and they are equally reliable; the first method is based on spectrophotometry and requires a large amount of serum, and the second method uses modified micro-bilirubin, which reduces the size of the required serum sample. [6,7] In addition, both procedures are invasive and cause pain, stress, and risk of infection for neonates. [8] Repeated blood sampling may lead to anaemia which may be a concern in low-birth-weight neonates. Trying to overcome these drawbacks, non-invasive methods of bilirubin measurements have been proposed. Transcutaneous bilirubinometer (TCB) has been shown to correlate with serum bilirubin. concentration in term infants. [3,9-11] It is reported that TCB reduced the need for blood sampling in neonates with visible jaundice. [12] TCB could also decrease the readmission rate for hyperbilirubinemia. [13,14] The purpose of our study is to assess the diagnostic accuracy of TCB compared with the total serum bilirubin (TSB) measurement in infants more than and equal to 35 weeks at different sites during the neonatal period and implementation of the results for better management of jaundiced neonates.

Material & Methods

This is a prospective, observational, cross sectional, hospital based study done on newborn babies between 350/7 weeks to 416/7 weeks of gestation for the duration of 12 months at Department of Pathology and Neonatology, Yashvi Children Hospital, Patna, Bihar, India . 200 neonates were included in the study.

Inclusion Criteria: Age of 2 to 7 days of life, born after >35 weeks gestational age, visible jaundiced neonates born with birth weight >2500 gm were included in the study.

Exclusion Criteria: Neonates who were under phototherapy, having exchange transfusion, babies with direct hyperbilirubinemia, babies with sepsis, hemangiomas, ecchymosis on forehead and sternum, Rh and ABO incompatibilities, babies with major congenital anomalies, TCB showing (no numerical value).

Methodology

370 newborns fulfilling the inclusion/exclusion criteria were taken into the study. Total 3040 live births occurred during study period with 2543 (83.65%) term, 301 (9.90%) late preterms.600 jaundiced newborns (>35-42 weeks) were enrolled, out of which 370 were included in study sample and rest were excluded who didn't match the study criteria. They were subdivided into 35-37 weeks, 37-40 weeks and 40-42 weeks groups. Each neonate was checked in broad day light for jaundice. Clinical staging of hyperbilirubinemia as per Kramer's staging were recorded. A detailed clinical assessment of the jaundiced neonates was done thoroughly. TCB determinations were made with the DRAGER JM-103, a hand-held bilirubinometer. All the measurements were performed with the same device on the forehead and mid sternum by single trained physician. Average of 3 measurements at both sites, reported as a numerical value were taken over a period of less than 60 seconds, simultaneously blood samples for TSB, direct and indirect bilirubin measurements were collected by venepuncture. These procedures were performed within 30 minutes of TCB measurements. TSB measurements were done by the skilled staffs of the bio chemistry laboratory by spectrophotometric method.

Statistical Analysis: The recorded values were plotted on Bhutani's nomogram with respect to hours of life. The information collected was tabulated and the data was analyzed using the software SPSS 18 for windows. Percentage, frequency and Chi-square test were used**.**

Results

Table 1: Sample distribution

Parameters	Mean	SD	95% confidenceInterval
Birth weight	2992.8	384.66	2906.39-2986.01
Gestationalage	38.64	1.56	38.47-38.79
Age (hours)	74.6	32.68	71.87-78.93
TCB (F)	12.38	3.16	12.02-12.66
TCB (ST)	12.32	3.14	11.97-12.71
TSB	12.98	3.57	11.6-12.32

The mean birth weight of the sample is 2992 gm (95% CI-2906.39-2986.01) with a standard deviation of 390.7 gm. The neonate with minimum weight in the study population was of 2505 gm and maximum of 4000 gm. Mean transcutaneous bilirubin level measured at forehead is 12.38 mg/dl (95% confidence Interval-12.02-12.66) with a SD of 3.16 mg/dl. Mean transcutaneous bilirubin level measured at sternum is 12.32 mg/dl (95% confidence Interval-11.97-12.71) with a SD of 3.14

mg/dl. Mean serum bilirubin level is 12.98 mg/dl (95% confidence Interval-11.6-12.32) with a SD of 3.57 mg/dl.

Table 2: Correlation between TCB and TSB at forehead and sternum for whole sample

Parameters	Karl Pearson's correlationco-efficient (r)	P value
TCB F	0.958	0.0001
TCB ST		
TCB F	0.960	0.0001
TSB		
TCB ST	0.920	0.0001
TSB		

The correlation between the readings of serum and transcutaneous bilirubinometer <15 mg/dl is very high at forehead (r=0.96, p=0.001) and sternum (r=0.92, p=0.001).

Table 3: Distribution according to Kramer's staging (visual assessment of jaundice)

Kramer ST	N	%
1	8	4
2	28	14
3	60	30
4	50	25
5	54	27

Our observation on visual assessment of jaundiced neonates 4% fall in Kramer's stage 1, about 14% are found in Kramer stage 2, In stage 3 highest percentage 30% (n=60) of neonates are falling in, 25% (n=50) found in stage 4 and in a stage 5. 27% (n=54) neonates are seen.

Table 4: Sensitivity and specificity of TCB in jaundiced neonates in different risk zones aged >120 hours

Statistics	Value (%)
Sensitivity	100
Specificity	78.96

The sensitivity of TCB at sternum remains 100% at low-risk zone as well as at high-risk zone, when measured at >120-168 hrs of life.

Discussion

Newborns typically exhibit elevated bilirubin levels during their initial days of life, a condition known as Physiological Jaundice. However, this physiological jaundice can be exacerbated or prolonged due to various factors. Unconjugated (indirect) hyperbilirubinemia represents a prevalent and generally benign condition frequently observed in neonates. Jaundice (icterus neonatorum), manifests through noticeable effects on various bodily tissues. One of the prominent indicators is the impact it has on the skin, sclera (the white part of the eyes), and mucous membranes. This condition results from a metabolic imbalance where bilirubin synthesis surpasses hepatic-enteric bilirubin clearance. The immaturity of the neonate's blood-brain barrier renders it permeable to a substantial bilirubin influx into the brain, thereby posing the potential risk of inducing a spectrum of irreversible cerebral injuries. These injuries may progress to acute bilirubin encephalopathy and culminate in kernicterus, a chronic form of bilirubin encephalopathy. Neonatal Jaundice impacts a significant portion of the neonatal cohort, affecting approximately 60% of full-term infants and 80% of preterm infants. [3,15]

The mean birth weight of the sample is 2992 gm (95% CI-2906.39-2986.01) with a standard deviation of 390.7 gm. The neonate with minimum weight in the study population was of 2505 gm and maximum of 4000 gm. Mean transcutaneous bilirubin level measured at forehead is 12.38 mg/dl (95% confidence Interval-12.02-12.66) with a SD of 3.16 mg/dl. Mean transcutaneous bilirubin level measured at sternum is 12.32 mg/dl (95% confidence Interval-11.97-12.71) with a SD of 3.14 mg/dl. Weerakul et al studied on 195 healthy term neonates of gestational age 37 weeks and birth weight greater than 2,500 grams using JM-103.The mean TCB was 9.5±2.4 mg/dl and the mean serum bilirubin was 10.5 ±2.5 mg/dl. [16] Gupta et al conducted their study by using JM-103, similar to the transcutaneous bilirubinometer, which we have used in our study. [17] National academy of clinical biochemistry laboratory medicine practice guidelines recommend Bilicheck and JM-103 for use in clinical setting. [18,19] Reliability and accuracy of transcutaneous bilirubinometers in comparison to serum bilirubin. Noninvasive transcutaneous bilirubin assessment by JM- 103 has demonstrated significant correlation when compared to total serum bilirubin measured by laboratory method.

Mean serum bilirubin level is 12.98 mg/dl (95% confidence Interval-11.6-12.32) with a SD of 3.57 mg/dl. The correlation between the readings of

serum and transcutaneous bilirubinometer <15 mg/dl is very high at forehead (r=0.96, p=0.001) and sternum (r=0.92, p=0.001). Hemmati et al also found a similar correlation between TCB and TSB (r=0.969, r(2)=0.94) at forehead. [20] Their sensitivity and specificity at the most reliable cut-off value (15 mg/dl) were 96.6% and 99%, respectively. Stillova et al found a close correlation (r=0.933) existing between TSB and TCB. [21] Janjindamai et al found a correlation coefficient (r)=0.95 in their study which is validates our study. [22] Kolman et al found that TCB correlates well with TSB in Hispanic neonates (r= 0.87). [23] In the study, Maisels et al[24] found a better correlation with TSB when TCB measurements were performed on the sternum (r=0.953) compared with the forehead (r=0.914).

Our observation on visual assessment of jaundiced neonates 4% fall in Kramer's stage 1, about 14% are found in Kramer stage 2, In stage 3 highest percentage 30% (n=60) of neonates are falling in, 25% (n=50) found in stage 4 and in a stage 5. 27% (n=54) neonates are seen. The sensitivity of TCB at sternum remains 100% at low risk zone as well as at high risk zone, when measured at >120-168 hrs of life. The differences between the TCB and TSB measurements with rising bilirubin values, agrees with the study done by Maisels et al. [24] In the present study, evidence is not sufficient to abandon neonatal serum bilirubin testing and replace it with TCB. NICE guidelines recommends that TCB is reliable in neonates whose serum bilirubin level was below 250μmol/l. [25] There is lack of data on the reliability of transcutaneous estimation of bilirubin at levels above 250 μmol/l.

Conclusion

The findings of the present study indicate that the TCB is a reliable screening tool for hyperbilirubinemia in newborns >35 weeks of gestation, especially with bilirubin levels ≤15 mg/dl in 2 -7 days of life. Although the measurement of TSB remains the gold standard for assessment of neonatal jaundice, TCB can be a viable option for universal screening. Correlation between TCB and TSB is not good above 15 mg/dl. TSB measurement should be performed if TCB is higher than 15 mg/dl. With regards to the site for using TCB, our study showed both forehead and sternum readings correlate well. The use of TCB along with 75th percentile of Bhutani's nomogram as a screening method in neonates would reduce the use of invasive methods and it will also allow starting treatment more promptly.

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