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Original Research Article

Comparative study between serum and transcutaneous bilirubin measurements in new-borns

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ABSTRACT

Background: Hyperbilirubinemia is one of the common problems in neonates. The transcutaneous bilirubin (TCB) measurement is non-invasive, easy and rapid not requiring expertise and manpower. Fewer studies have been carried out to whether newer TCB measurements can correlate with serum bilirubin measurements using newer generation of transcutaneous bilirubinometer in our region.
Methods: An observational cross-sectional study to compare serum and transcutaneous bilirubin measurements in newborns admitted to a neonatal intensive care unit, conducted from December 2015 to November 2017. Blood samples were obtained from neonates collected from venous sample into plain bulb and sent for analysis. For transcutaneous bilirubin measurement, the reading from forehead and sternum were taken using bilirubinometer and an average reading was taken for comparison.
Results: Total 172 neonates were admitted during study period and enrolled in the study. It was observed that out of 172 patients, studied 102(59%) patients were male and 70(41%) patients were female. Out of 172 patients maximum 89(51.74%) mother have O positive blood group and only 2(1.1%) have O negative blood group. Common cause of neonatal hyperbilirubinemia was ABO incompatibility 81(48%), Rh incompatibility 11(6%), and other causes 80(46%). The mean and standard deviation of TSB for first, second and third reading were 19.21±3.44, 15.76±2.79 and 12.89±2.44 respectively. While mean and standard deviation of TCB for first, second and third reading were 18.34±2.99, 15.48±2.36 and 12.31±2.28 respectively with correlation coefficient of r=0.806513, r=0.694273, r=0.785471 respectively indicating linear relationship between two.
Conclusions: There was a strong correlation between serum and transcutaneous bilirubin levels before and even after the phototherapy. As transcutaneous bilirubin estimation is non-invasive, gives quick and reproducible results. So, by using this method has potential screening value especially in the high-risk neonates to start early intervention.

Keywords: Bilirubin, Neonate, Total serum bilirubin, Transcutaneous bilirubin

INTRODUCTION

Hyperbilirubinemia is one of the common problems in neonates. Jaundice is observed during the 1st week after birth in approximately 60% of term infants and 80% of preterm infants. The yellowish discoloration is due to the accumulation of unconjugated, non-polar, lipid-soluble bilirubin pigment in the skin.[1] The determination of total serum bilirubin (TSB) levels is an invasive, costly and time-consuming work and require hospitalization and manpower. Moreover, repeated blood samplings may lead to significant blood loss leading to anemia, sepsis, pain and stress. On the contrary, the transcutaneous bilirubin (TCB) measurement is non-invasive, easy and rapid not requiring expertise and manpower. It is reported that TCB reduced the need for blood sampling in

neonates with visible jaundice and early management can be started so that complications and longer stay in hospital can be avoided which leads to decreased morbidity and mortality as well as the socio-economic burden on family.[2,3]

Transcutaneous bilirubinometry (TCB) was introduced into clinical practice in 1980 by Yamanouchi et al, using a bilirubinometer developed by Minolta.[4] This meter used a two-filter design to measure a "hemoglobin corrected yellow color." Because of the variability of the correlation of TCB readings and serum bilirubin concentration, use of TCB has been shown to result in a significant decrease in the need for serum bilirubin determinations.[5] Neonatal skin color and thickness represent important variables in TCB measurements. The variability between transcutaneous bilirubin and total serum bilirubin (TSB) measurements are related to other pigments in the skin, especially melanin and haemoglobin.[6]

The newer generation of transcutaneous bilirubinometer has a dual optical path system enables the machine to measure the bilirubin accumulated in deeper subcutaneous tissue while reducing the influence of melanin pigment and skin maturity.[7] So they can decrease the variability in the measurement of bilirubin. Fewer studies have been carried out to whether newer TCB measurements can correlate with serum TCB measurements in this region.

Hence the present study was planned with the objective to determine whether TCB measurements, as, correlate with TSB levels and whether TCB measurements obtained from the forehead and sternum generate comparable results so as to provide early and effective health care services in order to prevent disabilities and its socioeconomic burden on family and health care system.

METHODS

This was an observational cross-sectional study to compare serum and transcutaneous bilirubin measurements in newborns admitted to the neonatal intensive care unit by measuring serum bilirubin level and transcutaneous bilirubinometer level at tertiary care hospital.

The study was carried out between periods of December 2015 to the November 2017 at neonatal intensive care unit of SRTR GMC, Ambajogai, a tertiary care hospital after approval from local Institutional Ethics Committee.

Inclusion criteria

- All newborn infants admitted in neonatal intensive care unit of tertiary care hospital with hyperbilirubinemia willing to participate in the study were included in the study.

The parents of the newborn were informed regarding the study and informed consent was obtained from parents before starting the study and before collection of blood from newborns.

Exclusion criteria

- Neonate with sepsis, direct hyperbilirubinemia, major congenital anomaly, shock, hemangioma or ecchymosis on the forehead, previous phototherapy, blood exchange transfusion, birth asphyxia, skin diseases were excluded from study.

Stastical analysis

The mean of the transcutaneous bilirubin was compared with the serum bilirubin concentration. The relationship between transcutaneous and serum bilirubin values was determined using linear regression analysis. The strength of this relationship was quantified by the Pearson correlation coefficients. Receiver operating curve (ROC) was used to assess sensitivity and specificity before and after phototherapy and area under curve. Excel (Microsoft office excel 2007) and Medcalc version 16.8.4 were used for statistical calculations and graphs.

Data was collected using pre-tested semi structured proforma. Neonatal data collected including age, sex, birth weight, current weight, length, onset of jaundice, birth order in the family, history of jaundice in the family, type of feeding, history of hospitalization, neonatal and maternal blood group, history of phototherapy, Previous measurements in serum and skin bilirubin, history of blood transfusion in new-born, and maternal prenatal care. Serum sample both bilirubin levels reading serum and transcutaneous were taken simultaneously. Blood samples were obtained from neonates collected from venous sample into plain bulb.

The samples were immediately sent to the hospital laboratory where the serum was separated and then immediately assayed for bilirubin by a DIAZO method which involves reacting serum with diazo reagent and then through spectrophotometry the levels of direct and indirect bilirubin are determined. Transcutaneous bilirubin level measurement was done by a single transcutaneous bilirubinometer used throughout the study period.

The optic head of the meter is gently pressed against the neonate’s skin (usually forehead or upper part of the sternum). For correct measurement, the optic head should make full contact with the skin and there should be no gaps between the head and the skin. This should be achieved by gentle pressure. The reading from forehead and sternum were measure and an average reading taken for comparison. After taking first reading babies kept on phototherapy and patch cover of an area approximately 1.5cm^2 were applied over forehead and sternum and a

second reading is taken after 24 hour and third reading thereafter by the same way.

RESULTS

The present study was carried out in 172 cases of neonatal jaundice to compare serum and transcutaneous bilirubin level in newborns. The following observations were made.

According to gestational age, out of 172 patient of neonatal jaundice 45(26%) was preterm, 122 (70.93%) were term and 5 (2.9%) were post-term baby. It was observed that out of 172 patients, studied 102(59%) patients were male neonatal jaundice and 70(41%) patients were female neonatal jaundice. The male to female ratio was 1.45:1.

Table 1: Blood groups of the mothers.

Mother blood group	No. of mothers
A $^{+}$ve	21 (12.2%)
B $^{+}$ve	39 (22.67%)
AB $^{+}$ve	12 (6.9%)
O $^{+}$ve	89 (51.74%)
A^{-}ve	3 (1.7%)
B^{-}ve	6 (3.4%)
O^{-}ve	2 (1.1%)

According to postnatal age at the time of admission 22 (12.8%) patients present within first two days, 131(76.17%) present within 3-7 days. Overall 153(88.9%) patients present in the first week of life and 19 (11.04%) after 1 week. It was observed that out of 172 patients 8.14% were very low birth weight baby, 31.39% low birth weight and 60.47% were above 2.5kilograms. As shown in the Table 1, out of 172 patients maximum 89 (51.74%) mother have O positive blood group and 2(1.1%) minimum have O negative blood group shows the blood group of mothers

Table 2: Blood groups of the patients/new-borns.

Patient blood group	No. of patients
A $^{+}$ve	62 (36%)
B $^{+}$ve	91 (52.9%)
AB $^{+}$ve	03 (1.7%)
O $^{+}$ve	14 (8.13%)
A^{-}ve	2 (1.1%)

As shown in the Table 2, out of 172 patients, maximum 91(52.9%) neonates have blood group B positive and minimum 2 (1.1%) patients have A negative blood groups.

Most common cause of neonatal hyperbilirubinemia was ABO incompatibility 81 (48%), Rh incompatibility accounted for 11 (6%), other cause accounted for 80 (46%).

Table 3: Mean serum and transcutaneous bilirubin at various points.

TSB/TCB	Mean serum bilirubin (MG/DL)	Mean transcutaneous bilirubin (MG/DL)	Correlation coefficient
First	19.21+3.447	18.34+2.99	R=0.806513
Second	15.76+2.79	15.48+2.36	R=0.694273
Third	12.89+2.44	12.31+2.28	R=0.785471

It was observed that 19 (11.04%) patients have serum bilirubin level on admission less than 15mg/dl, 89(51.74%) patients have between 16-20mg /dl and 64 (37.2%) patients have the level above 20mg /dl. It was observed that 29 (16.86%) patients have transcutaneous level <15mg /dl, 104 (60.46%) patients have between 16-20mg /dl and 39 (22.67%) patients have level above 20 mg /dl. Table 3 shows that mean and standard deviation of TSB for first, second and third reading were 19.21±3.44, 15.76±2.79 and 12.89±2.44 respectively. While mean and standard deviation of TCB for first, second and third reading were 18.34±2.99,15.48±2.36 and12.31±2.28 respectively.

Figure 2 shows that there is a linear relationship between serum bilirubin concentration and transcutaneous bilirubin concentration with R^2 = 0.482 and r=0.694273 (P <0.0001) taken after starting phototherapy.

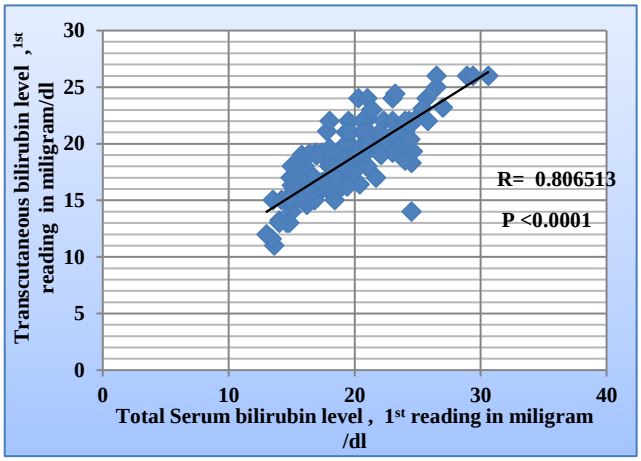

Figure 1: Scatter plot depicting correlation between TSB and TCB (first reading).

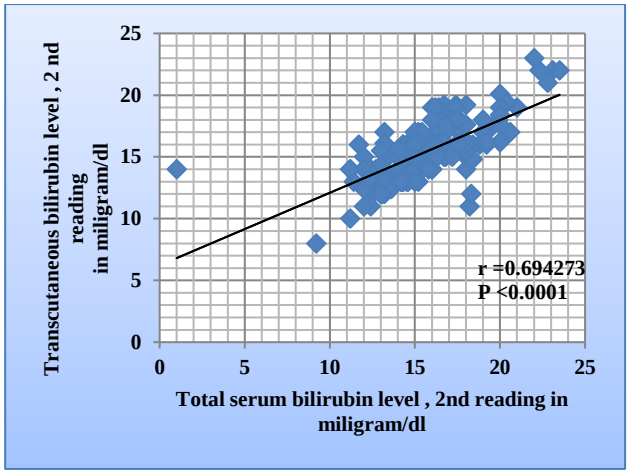

Figure 2: Scatter plot depicting correlation between TSB and TCB (second reading).

Figure 3 shows that there is a linear relationship between serum bilirubin concentration and transcutaneous bilirubin concentration with $R^2 = 0.617$ and r =0.785471 (P <0.0001) second reading after starting phototherapy.

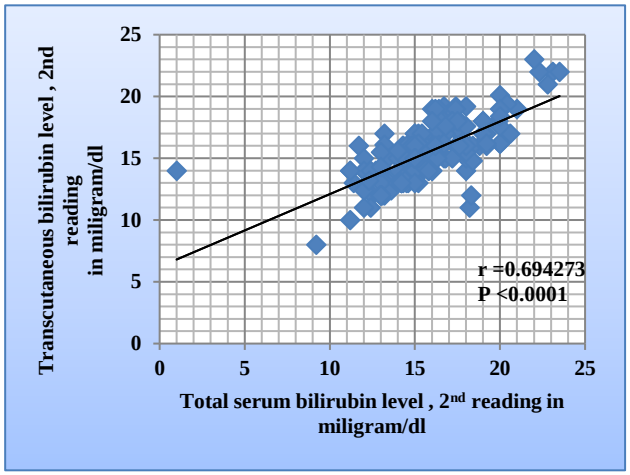

Figure 3: Scatter plot depicting correlation between TSB and TCB (third reading).

DISCUSSION

Transcutaneous bilirubinometer is regarded as a sensitive screening method for hyperbilirubinemia in term or preterm newborn. However, there were few studies about of transcutaneous bilirubinometer in the Indian population. So, we conducted an observational study to compare the correlation between serum and transcutaneous bilirubin measurement in neonates presented with hyperbilirubinemia satisfying the inclusion and exclusion criteria

In the present study out of 172 babies 122 (71%) babies were in the gestational age group of 37 to 41 weeks and only 2 (1%) babies were less than 32 weeks of gestation. Observation made above suggest that there is high prevalence of hyperbilirubinemia among term babies which is in concordance with the study done by Karen T et al, that showed out of 150 babies, 99 (66%) were term babies, 38 (25%) were preterm babies between gestational age of 34-36 weeks, and finally 13 (8%)were preterm babies ≤33 weeks.[8] Another study conducted by Shah B et al, showed that of 430 babies 250 (59%) were term and 180 (41%) babies were preterm.[9]

The present study showed that 131 (76%) neonates presented at a postnatal age between 3-7 days while 22 (13%) presented between day 1-2 of life and 19 (11%) presented after day 7 of life. Above findings conclude that most neonates with hyperbilirubinemia present in early neonatal life. Same observations were made by Sadik IA et al, which showed that 91.9% neonates developed jaundice during the period of 2-7 days while 5.9% on the first day and 2.6% after a week.[10] In a study by Mansouri M et al, observed that out of the 200 neonates, 124 (62%) were boys and 76 (38%) were girls, the results were in accordance with our study which showed males were 102 (59%) and females were 70 (41%).[11]

In our study we found that 14 (8%) neonates were VLBW and 54 (32%) were LBW while 104 (60%) neonates were normal weight babies. These observations are similar to the study done by Akahira-Azuma M et al.[12] Observations made in our study showed that blood group of most of the mothers i.e. 89 (51%) was O^+ve further, 93% mothers were Rh^+ve and 7% were Rh^-ve. Most common blood group among the neonates in the study was B^+ve i.e. 53%. In our study most common cause of hyperbilirubinemia was ABO incompatibility seen in 81 (48%) neonates, Rh incompatibility was present in 11 (6%) babies and remaining 80 (46%) neonates had other cause of hyperbilirubinemia. Heier HE et al, study indicates that children of mothers with blood group O run a double risk of hyperbilirubinemia requiring treatment as compared to children of mothers of blood group A, and 5-10 times increased risk of needing exchange transfusion.[13] The most frequent cause of need for exchange transfusion was ABO-incompatibility between mother and child. Blood group O in the mother should be considered to be an independent risk factor for the child.

In our study most of the neonates presented with TSB and TCB less than 15 mg/dl 19 (11%) and 29 (17%), between 15-20mg/dl was 89 (52%) and 104 (64%), more than 20 mg/dl 64 (37%) and 39 (23%) respectively. Similar observations were made by Sadik IA et al, where TSB level among jaundiced neonates Less than 12 mg/dL was found in (29.4%), 12-2 mg/dL were detected in (67.9%), and More than 20 mg/dL was recorded in (2.6%).[10] While, TCB level less than 12 mg/dL found in (20.9%), 12-2 mg/dL detected in (77.1%) and more than 20 mg/dl cited for (1.9%). Other studies conducted by Seeralar A et al, showed similar results.[14] The present study shows that mean and standard deviation of TSB for first, second and third reading were 19.21±3.44, 15.76±2.79 and

12.89±2.44 respectively. The mean and standard deviation of TCB for first, second and third reading were 18.34±2.99, 15.48±2.36 and 12.31±2.28 respectively. Similar observations were made by Fatih Ş et al, Fonseca R et al, Canyang Z et al.[15-17] Observations made in our study show the coefficient of correlation (r) of TSB/TCB for readings taken before phototherapy is 0.80 ($p < 0.01$) while the coefficient of variance (R^2) is 0.65 ($p < 0.01$). It shows that there is the strong correlation between readings of TSB and TCB. The coefficient of correlation (r) of TSB/TCB for two readings taken after phototherapy are 0.69, 0.78 ($p < 0.01$) while coefficient of variance (R2) are 0.48, 0.61 ($p < 0.01$). It shows that there is the strong correlation between readings of TSB and TCB even after phototherapy. These observations are in concordance with the studies done by Shah B et al, which also shows that there was a strong correlation between plasma and mean transcutaneous bilirubin assay measured (CV=0.49, r=0.8599, $p<0.001$).[9] There were no correlation between plasma and transcutaneous bilirubin in group-1(CV=0.15,r=0.3450,$p>0.001$) and group-2 (CV=0.18,r=0.4521,$p>0.001$) suggestive of wide variation in transcutaneous bilirubin value and serum bilirubin value.

Panburana J et al, studied that the TCB and TSB values had linear correlation with significant correlation coefficient (r 0.81, $p < 0.001$).[18] The correlation equation was TSB=0.88+0.89 x TCB (r^2=0.65). TCB levels tended be higher than TSB with mean difference of 0.44 mg/dL (95% CI: 0.74330.1323mg/dL) and SD:1.64. Fatih MŞ et al, study also shows that there was a good correlation between transcutaneous bilirubin and total serum bilirubin measurements (Pearson's correlation coefficient 0.87 for TCB from the forehead, 0.88 for TCB from the sternum; $p<0.001$).[15] Study conducted by Akahira-Azuma M et al, also shows similar results.[12]

Above discussion shows that there is a significant correlation between serum and transcutaneous bilirubin levels before and even after the phototherapy. As transcutaneous bilirubin estimation is non-invasive, gives quick and reproducible results require minimum expertise, this method should be used regularly to screen the neonates presenting with neonatal hyperbilirubinemia.

CONCLUSION

In this comparative study of serum and transcutaneous bilirubin measurements in new-borns done in tertiary care hospital, we found that there was a strong correlation between serum and transcutaneous bilirubin levels before and even after the phototherapy. As transcutaneous bilirubin estimation is non-invasive, gives quick and reproducible results.

So, by using this method we can easily screen out the high-risk neonates and start early intervention. This can significantly reduce the morbidity and mortality in neonates and in turn its socioeconomic burden on family and health care system.

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