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Investigation of correlation study among transcutaneous and total serum bilirubin content in preterm neonates

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ABSTRACT

Background. Neonatal jaundice is a commonly occurring problem in both full term and preterm neonates. It is one of the major causes for neonatal mortality and morbidity.

Objective. To assess the correlation among transcutaneous bilirubinometer readings and Total serum bilirubin levels at different sites in early and late preterm neonates before and at the end of phototherapy.

Method. An observational study was conducted in preterm neonates diagnosed with jaundice. The Transcutaneous Bilirubin (TCB) instrument, Drager JM105 is used to assess TCB and it was recorded on three sites and average of the three readings was noted. Prior to phototherapy, TCB was noted 30 min before TSB was sent. A photo-opaque patch was placed on the sternum and phototherapy was given. At the end of the phototherapy, TCB on the sternum was noted and then TSB was sent with a time gap of not more than 30 min.

Results. In this study, out of 50 neonates 14 were early preterm and 36 were late preterm babies. It was found that there was a positive correlation between TCB and TSB in early preterm babies before phototherapy (p value=0.0019), but there was no correlation between TCB and TSB at the end of phototherapy. In late preterm babies there was no correlation between TCB and TSB both before phototherapy and at the end of phototherapy.

Conclusion. In this study it was found that TCB has positive correlation with TSB and can be implemented for the screening of hyperbilirubinemia even in preterm neonates.

Keywords: transcutaneous bilirubin, total serum bilirubin, neonatal jaundice, phototherapy, correlation

INTRODUCTION

Neonatal jaundice is one of the most common neonatal problems in 60% of the full-term and 85% of preterm neonates. The incidence of neonatal hyperbilirubinemia (NNH) in preterm infants requiring phototherapy is 60% in India [1]. Neonatal jaundice can sometimes make the newborn drowsy, and also affect the feeding. Severe jaundice can cause permanent neurological damage known as Kernicterus [2].In newborns, jaundice is assessed by using digital pressure to blanch the skin so that it reveals underlying skin and subcutaneous tissue and observing for the presence of apparent icteric sclera and yellowish discoloration of face which extended down onto chest and extremities. But, the physical examination of jaundice in the neonates with the naked eye can be inconsistent. The exact correlation of serum bilirubin which remains gold standard for estimation of bilirubinemia with the appearance of the skin color as yellowness in jaundice is fraught with irregularities and mistakes [3]. The rate of increase of serum bilirubin with clinical appearance of jaundice in the neonates was first published and later adopted for clinical assessment of jaundice by Kramer. According to this method,

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when serum bilirubin reaches 6 mg/dL the face is jaundiced, at serum bilirubin level <9 mg/dL the jaundice extends up to umbilicus, at the level 12 mg/dL, it extends up to knees and at the level, 15 mg/dL the jaundice extends up to the ankles and wrist and when jaundice appears on hands and feet, bilirubin is supposed to be >15 mg/dL.

Although this method is rapid and inexpensive, Kramer index is not very accurate when applied to neonates of diverse racial backgrounds [4]. Hyperbilirubinemia in neonates is of concern as it can lead to bilirubin induced neurological damage (BIND) due to Kernicterus and may lead to death if not treated on time. This damage to the brain is permanent and manifests as cerebral palsy. Hence it is essential to make a prompt diagnosis with proper modality of treatment [5]. Early detection, management and prevention of neonatal jaundice in healthy term and late preterm neonates remains a challenge, still it common and its complication, Kernicterus is a rare occurrence in India i.e. in a research in north India, Kernicterus occurred in 9.8% of infants with blood bilirubin levels between 20 and 25 mg/dl [6]. The estimation of serum bilirubin is done by withdrawing blood of the neonates each time when the analysis is clinically necessary according to protocol for management of NNH. While it is gold standard, the demerits include pain, infection, anemia and time. Transcutaneous bilirubinometry (TCB) is a non-invasive and reliable technique for the detection of hyperbilirubinemia which works on the principle of spectrophotometry. In order to analyze the spectrum of optical signals using photocell transcutaneous bilirubinometers were used. These are later converted to an electrical signal by a photocell. Later these electric signals are analyzed by a microprocessor which generates a bilirubin value on the LCD (Liquid Crystal Display). TCB is a measurement of tissue bilirubin. There are different varieties of transcutaneous bilirubinometers with unique operating procedures that work on the same principle. At present transcutaneous bilirubin (TCB) measurements are used for screening bilirubin values in icteric neonates more than 35 weeks [4]. This also has been proved to be reliable in neonates less than 35 weeks of gestation [5]. Also, for neonates with gestational age 28–34 + 6 weeks specific TCB cut off threshold levels were published, this was done in order to identify that specific neonate requiring total serum bilirubin (TSB) for confirming the requirement of phototherapy. This may cause skin bleaching which may result in false TCB reading, thus a photo-opaque patch is used to cover on the infant's forehead or sternum. It can shield the skin from the light during phototherapy, then the TCB reading can be taken from the covered site.

MATERIAL AND METHODS

A prospective observational study was conducted at Neonatology unit, Department of Pediatrics, Acharya Vinoba Bhave Rural Hospital (AVBRH), Sawangi (Meghe), a tertiary care hospital in rural Maharashtra from October 2019 to September 2021. The study included preterm neonates (=/>28 to <37 weeks of gestation) up to 14 days of life who required phototherapy. The exclusion criteria were those subjects whose parents were not willing to participate.

The present study was initiated after get the permission from the Institutional Ethics Committee (Reference no- DMIMS (DU)/IEC /Aug-2019/8240), Acharya Vinoba Bhave Rural Hospital, Jawaharlal Nehru Medical College, Sawangi (Meghe), Wardha. The study was performed after taking written consent from the parents. All the relevant information was gathered in the pre-designed proforma. Relevant maternal history was gathered which included maternal complications, mother's blood group, place of delivery and Perinatal factors like mode of delivery and requirement of resuscitation. Anthropometry, complete general and systemic examination with relevant investigations of TCB levels along with modality and duration of treatment with cause and immediate outcome was entered in a pre-validated proforma. The TCB instrument, Drager JM105 was used after calibration [7]. The TCB was recorded on three sites namely forehead, sternum and pubic symphysis before phototherapy. Average of the three readings was noted. Then a serum sample was sent to laboratory for Total Serum Bilirubin estimation in a plain bulb within 30 minutes of measurement of TCB. Then the neonate was covered with a non-penetrating patchover the sternum using a circular barrier (1 cm in diameter) made of maxicor electrode covered with aluminium foil and a transparent semipermeable dressing (aluminium foil has been proven to protect the skin from PT) during the phototherapy. At the end of phototherapy TCB over the covered area of the sternum was noted and another sample of TSB was sent for analysis with a time difference of not more than 30 minutes. The correlation between TSB and TCB was measured before and at the end of phototherapy.

Statistical analysis

The obtained data was entered in the Microsoft EXCEL spreadsheet and the final analysis was done with the use of SPSS software, version 21.0. Qualitative data was analyzed using frequency and percentages. Quantitative data was analyzed using mean and standard deviation. Pearson correlation was used to evaluate the correlation between TSB and TCB. For statistical significance, p value of less than 0.05 was considered statistically significant.

The readings were repeated three times and standard deviation (SD) was calculated.

RESULTS

In the present study, 50 Preterm neonates (n=50) were diagnosed with NNH and admitted to the NICU of our hospital for phototherapy. Table 1 showed the hyperbilirubinemia in Preterm Neonates irrespective of male and female Neonates.

TABLE 1. Sex distribution in Preterm Neonates with Hyperbilirubinemia

Sex	Observation (n=138) (%)
Males	32 (64%)
Females	18 (36%)
Total	50 (100%)

Above table shows the sex distribution in Preterm Neonates with Hyperbilirubinemia. Out of 50 Preterm neonates that were involved in the study, 32 (64%) were males, while 18 (36%) were females. The study showed the male and female ratio of Neonates as 1.77:1 with the coefficient of determination (R^2) value of 1 (Figure 1).

Further, an effect of Gestational age was correlated with TSB and TCB in preterm neonates with Hyperbilirubinemia (Table 2).

TABLE 2. Effect of Gestational age on correlation of TSB and TCB in preterm neonates with Hyperbilirubinemia

Gestational age	Early Pre-term	Late Pre-term
Total Serum bilirubin	13.86 ± 1.65	13.29 ± 1.94
Transcutaneous bilirubin	12.79 ± 1.70	12.74 ± 1.99
p value	0.001*	0.000*
r value	0.826	0.869

*- significant (p<0.05); Mean ± SD; where, n =3, SD = Standard deviation

Above table shows positive correlation between TSB and TCB in early and late preterm neonates with Hyperbilirubinemia.

Thereafter, total 50 neonates were tested for total serum bilirubin and transcutaneous bilirubin content where 11 neonates exhibited ABO incompatibility. The result was tabulated in table 3. The table 3 also showed the ABO incompatibility is significantly associated with Total serum bilirubin levels but not with Transcutaneous bilirubin.

TABLE 3. Effect of ABO incompatibility on TSB and TCB in preterm neonates with Hyperbilirubinemia

ABO incompatibility	Total Serum bilirubin bilirubin (n=50)	Transcutaneous bilirubin (n=50)
Absent	13.17 ± 1.72	12.49 ± 1.84
Present	14.43 ± 2.11	13.70 ± 1.86
p value	0.04*	0.06

*significant (p<0.05); Mean ± SD; where, n =3, SD = Standard deviation

Furthermore, correlation study between TCB readings at different sites (forehead, sternum and pubis) and TSB before phototherapy was performed and resulted significant (p<0.05) positive correlation (Table 4). Henceforth, correlation study also showed significant positive result when correlated between TCB and TSB before and after phototherapy (Table 5).

TABLE 4. Correlation between Transcutaneous bilirubinometer readings at different sites of forehead, sternum and pubis and Total serum Bilirubin before phototherapy

Sites	Transcutaneous bilirubin (n=50)	Total serum Bilirubin (n=50)	p value	r value
Forehead	13.10 ± 1.98	13.45 ± 1.86	0.001*	0.872
Sternum	13.01 ± 1.92		0.001*	0.859
Pubis	12.2 ± 1.84		0.000*	0.779

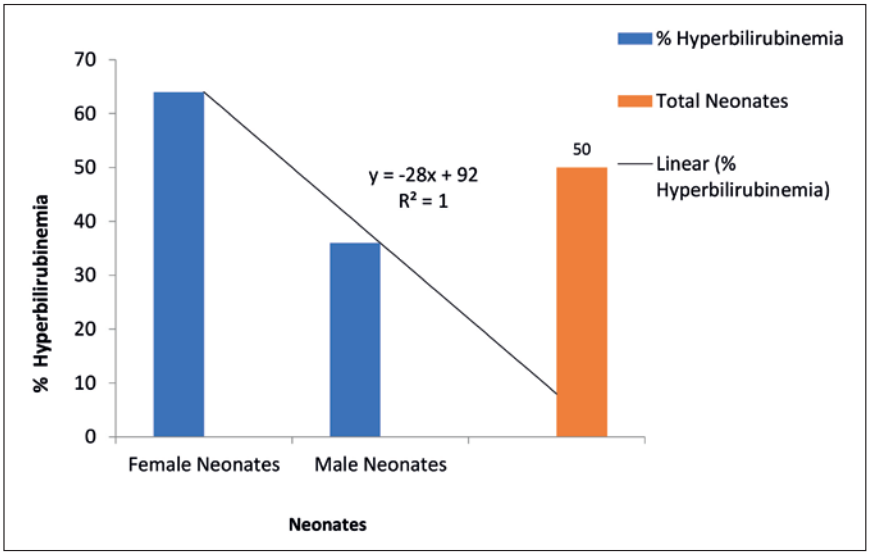

FIGURE 1. Coefficient of determination (R^2) value in Neonates with Hyperbilirubinemia

TABLE 5. Correlation between TCB and TSB before phototherapy and on sternum at the end of phototherapy in preterm neonates with Hyperbilirubinemia

Bilirubin Estimation	Before Phototherapy (n=50)	At the end of phototherapy (n=50) (on covered sternum)
TSB	13.45 ± 1.86	6.59 ± 2.47
TCB	12.75 ± 1.89	6.48 ± 2.34
p value	0.000*	0.001*
r value	0.853	0.992

*significant (p <0.05); Mean ± SD; where, n = 3, SD = Standard deviation

DISCUSSION

Hyperbilirubinemia is a common neonatal condition which is a result of imbalance between rate of formation and rate of elimination of bilirubin. It is usually observed in the first week of life in 60% term and 85% preterm neonates [8,9]. The incidence is more in preterm neonates owing to the developmentally immature liver and gastrointestinal tract that is unable to excrete bilirubin as fast as it is formed. This leads to accumulation of bilirubin in the body [10].

Unmanaged hyperbilirubinemia can cause irreversible brain damage, "Kernicterus", which is associated with yellow staining of basal ganglia resulting in permanent and long-term neurological sequelae in a developing brain [11]. It is therefore essential to diagnose hyperbilirubinemia before it causes neurological sequelae, and a quick and easy mode of diagnosis is essential. TCB is the newer and quicker method of bilirubin estimation. It overcomes the pain of trauma and repeated blood sampling in neonates for serum bilirubin analysis.

Present study was performed to identify the correlation of the total serum bilirubin with that of transcutaneous bilirubin in preterm neonates with hyperbilirubinemia. In our study, the ratio of males: females were 1.77:1 which was similar to a study conducted by Raba et al., [12] where it was reported with a total of 105 males (53.6%) and 91 females (46.4%) with the ratio of 1.2:1. and to a study conducted by Jnah et al., [13] in which number of males were 25(55.6%), while the number of females was 20 (44.4%) and male: female ratio was 1.25:1.

In this study, out of 50 neonates 14 were early preterm and 36 were late preterm babies and it was found that there was a positive correlation between TCB and TSB in early preterm babies before phototherapy (p value = 0.0019), whereas there was no correlation between TCB and TSB at the end of phototherapy. In late preterm babies there was no correlation between TCB and TSB both before phototherapy and at the end of phototherapy.

In a study by Pendse et al, [14] it was found that preterm neonates between 28-32 weeks of gestation showed better TCB v/s TSB correlation before and after phototherapy than in preterms between 32-37 weeks of gestation. In another study by Panda et al. [15] TCB is correlated with TSB before phototherapy better in early preterms than in late preterms which is similar to our study.

In the present study, birth weight does not affect the correlation between TCB and TSB before and during phototherapy. In a study by Hulzebos et al. [16], neonates having a weight more than 2000 g had the highest mean TSB levels which was in contrary to this where the highest mean TSB was found to be in <1000 g (ELBW) neonates. The mean difference between TSB and TCB levels was found to be similar for all the studied birth weight categories which were similar to this study.

In the present investigation, out of 50 preterm neonates, 11(22%) babies had ABO incompatibility-and it was found that there was significant association between ABO incompatibility and occurrence of NNH which was similar to a study conducted by Kalakheti et al., [17] in which there was 2.6 times higher risk of neonatal jaundice in neonates with ABO incompatibility.

Thereafter, in the study, the positive correlation between mean TCB on all the sites (forehead, sternum and pubis) and mean TSB was resulted. The similar study was also reported by earlier researches where mean TCB at forehead and mean TSB was almost similar when compared to other sites [18-20].

CONCLUSION

In this study it was found that there was positive correlation between TCB and TSB in both early and later preterm neonates; and at both before and at the end of phototherapy. Positive correlation was also found between TCB readings at different sites (forehead, sternum and pubis) and TSB before phototherapy. The transcutaneous bilirubinometry served as a reliable technique for detecting neonatal jaundice. Therefore, the study finally revealed that TCB can be used for screening of hyperbilirubinemia in preterm neonates, enabling minimal handling of preterm neonates and reduction of iatrogenic blood loss and also for prompt treatment of neonatal jaundice.

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