

ORIGINAL RESEARCH ARTICLE

COMPARISON OF TOTAL SERUM BILIRUBIN AND TRANSCUTANEOUS BILIRUBIN IN NEONATES WITH HYPERBILIRUBINAEMIA

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Received: 05 Feb, 2022

Accepted: 08 Mar, 2022

Published: 15 Mar, 2022

Key words: Jaundice; Neonate; Serum Bilirubin; Transcutaneous bilirubinometer.

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DOI: <https://doi.org/10.54530/jcmc.670>

Citation

Shrestha S, Shrestha BM, Prajapati B. Comparison of total serum bilirubin and transcutaneous bilirubin in neonates with hyperbilirubinaemia. Journal of Chitwan Medical College. 2022;12(39):121-5.

ABSTRACT

Background: Jaundice is considered as one of the most prevalent and common clinical problems during neonatal period which may require interventional treatment. Transcutaneous bilirubinometry is a simple method for estimating bilirubin levels and diagnosing jaundice in neonates. This study was done to compare transcutaneous bilirubin and total serum bilirubin in jaundiced neonates.

Methods: A hospital based prospective cross-sectional study of neonates from Out Patient Department, Emergency Ward, and Neonatal Intensive Care Unit with clinical jaundice was conducted between January 2016 and December 2016, at Kanti Children's Hospital, Maharajgunj, Nepal. A total of 162 neonates were interviewed using preformed questionnaires. Then the correlation between the transcutaneous bilirubin and plasma bilirubin level was assessed by linear regression analysis. It was then analyzed with the help of SPSS Version 20. p-value <0.05 was considered statistically significant.

Results: Out of 162 cases, 61.7% were males and 38.3% were females. There was a high correlation between TcB and TSB level in neonates ($r = 0.981$) and this finding was statistically significant ($p\text{-value} < 0.001$). Correlation coefficient of 0.98 and 0.97 were found in term and preterm neonates respectively, which suggested strong correlation between TcB and TSB in both groups of neonates.

Conclusions: Transcutaneous bilirubin measurement can be considered as a suitable tool for predicting neonatal bilirubinemia as it has high sensitivity.



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INTRODUCTION

Jaundice or hyperbilirubinemia is a common and in most of the cases benign problem in neonates.¹ It is defined as yellowish discoloration of the sclera and body due to presence of high bilirubin level in blood. Bilirubin pigment gets deposited in different tissues of the body and the baby looks icteric (jaundiced). In adults, normal serum bilirubin is less than 1 mg/dl, but they appear icteric when serum bilirubin level is more than 2 mg/dl. Newborns appear icteric when serum bilirubin level is more than 7 mg/dl.² Jaundice is observed in approximately 60% of term infants and 80% of preterm infants during the first week after birth.¹ About 6.1% of well term newborns have maximum serum bilirubin level > 12.9 mg/dl. 3% of normal term babies have serum bilirubin level >15 mg/dl.¹

Elevation of indirect (unconjugated) bilirubin is potentially neurotoxic, although bilirubin plays a role as an antioxidant. It can lead to kernicterus, acute and chronic bilirubin encephalopathy with focal neurological deficit (e.g. sensory neural hearing loss) and neurobehavioral problems in

neonates.^{3,4} So, early identification and recognition is necessary to check further rise of serum bilirubin.

Measuring bilirubin levels is vital for the better treatment of neonatal jaundice, which is usually done by visual, cutaneous, and serum evaluations.⁵ Total serum bilirubin (TSB) measurement is a standard method of measurement but it can lead to complications eg: infection, anaemia, pain, and stress because of frequent blood sampling. Also, this method is stressful, time consuming and expensive.²

In recent decades, non-invasive bilirubin measurements have been used in jaundiced patients that have helped in reducing patients' stress, laboratory expenses, and the need for frequent blood sampling. Transcutaneous bilirubinometry is one of these noninvasive methods.⁶ In this method, the bilirubin meter is pressed against the skin that causes pallor, and bilirubin levels are measured using light waves in different ways.^{7,8} This method is easy to perform and is pain-free for the infant, and also this test gives immediate results.⁹ It may be a useful screening device to decrease the risk and discomfort associated with blood sampling in neonates.

American Academy of Paediatrics (AAP) guidelines indicate that Transcutaneous bilirubin (TcB) measurements are mostly accurate in diagnosing neonatal jaundice, and can reduce the need for frequent blood sampling. Also, they have recommended that all neonates should undergo TSB or TcB measurements at least once before hospital discharge to assess their risk of jaundice.⁵

Determination of neonatal jaundice by transcutaneous bilirubinometry is not routinely done in Nepal as used commonly in European and other nations. The objective of the current study was to evaluate the accuracy of TcB measurements for assessing hyperbilirubinemia in the neonates, by using TSB as the reference standard.

METHODS

Following ethical approval from Institutional Review Board (IRB) of National Academy of Medical Sciences (ref no: 484/078/079) a hospital based prospective cross-sectional study was conducted January 2016 to December 2016 in the Out-Patient Department (OPD), Emergency (ER), Neonatal Intensive Care Unit (NICU) of Kanti Children's Hospital (KCH), Maharajgunj, Kathmandu, Nepal which is the only one central governmental tertiary referral center of Federal Republic Of Nepal. The sample size of 162 was calculated by using prevalence formula, $n = Z_{\alpha}^2 PQ / d^2$ where $Z_{\alpha} = 1.96$, $P = 12\%$ and $d = 5\%$.

All neonates with clinical jaundice were included whereas neonates who have prior received exchange transfusion or phototherapy, neonates with parents not giving consent and neonates who had skin infection and purpura and bruise at the site of TcB measurement were excluded.

They were enrolled after taking informed written consent from one of the parents or care taker. Neonates were examined by a paediatric resident, their bilirubin levels were measured on the forehead (midfrontal region) which was here used as the standard site.¹⁰ In this study, we used bilirubinometer (JM-105, Dräger manufactured by Draeger Medical Systems, Telford U.S.A) to measure transcutaneous bilirubin.

The mean levels were recorded and blood samples were obtained within 30 minutes and were sent to the laboratory for determining TSB. Total serum bilirubin estimation was measured by BR-501, a bilirubin meter machine which was made in Japan, 2010. The two measurements obtained from these two methods were then compared.

Data collection was done by using pre-designed proforma which included neonatal data including: age, sex, birth weight, current weight, onset of jaundice, history of phototherapy as well as routine blood test including total serum bilirubin along with transcutaneous bilirubin level measured at skull by bilirubinometer.

Data was then analyzed using SPSS (Statistical Package for Social Science) software, version 20. Independent t-test (to

compare the quantitative variable in the two studied groups) and Pearson's correlation coefficient (to evaluate effective parameter on dependent variable) was used accordingly. p-value <0.05 was considered statistically significant for this study.

RESULTS

Among 162 eligible neonates with neonatal hyperbilirubinemia, 100 (61.7 %) of them were male and 62 (38.3 %) were female with male: female ratio being 1.6:1.

Table 1: Table showing sex distribution (N=162)

Sex	Frequency (%)
Male	100 (61.75%)
Female	62 (38.3%)
Total	162 (100%)

Maximum number of neonates (64.2%) belonged to age group of 0-7 days which was followed by 37 (22.8%) neonates in age group 8-14 days. 16 (9.8%) neonates were from 15-21 days age group whereas 5 (3.1%) neonates were at 22-28 days of life.

Table 2: Table showing age wise distribution of study population (N=162)

Age (in days)	Male	Female	Frequency (%)
0-7	67(41.5%)	37(22.8%)	104 (64.3%)
8-14	20(12.3%)	17(10.5%)	37 (22.8%)
15-21	8(4.9%)	8(4.9%)	16 (9.8%)
22-28	5(3.1%)	0	5 (3.1%)
Total	100	62	162 (100%)

In our study, 130 (80.2%) neonates had birth weight between 2.5 and 4 kg. 28 (17.3%) neonates were below 2.5 kg and 4(2.5%) neonates had birth weight more than 4 kg.

The mean \pm SD serum and cutaneous bilirubin levels were 11.97 ± 4.12 and 12.76 ± 4.20 mg/dl respectively.

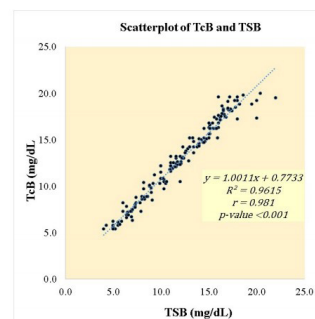


Figure 1: TSB versus TcB Measurements n=162 comparisons

A scatter plot was developed to see whether there exist any relationship between TcB and TSB. Using least square principle, a regression line was fitted to the data. A highly significant correlation $r = 0.981$ ($p < 0.001$) appeared.

Since residual plot is random, there is sufficient evidence that

a linear regression is a good fit for given data as explained by figure.

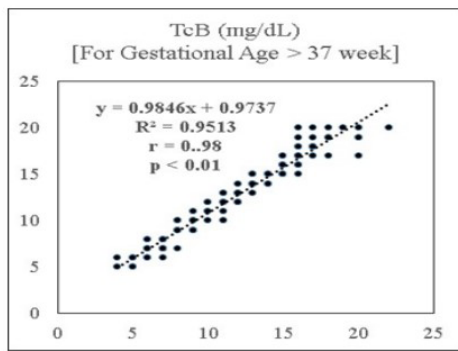


Figure 2: TSB versus TcB measurements in neonates more than 37 weeks of gestation

A highly significant correlation $r = 0.98$ ($p < 0.01$) was observed between TcB and TSB in neonates of gestational age more than 37 weeks (term neonates) as per figure 2.

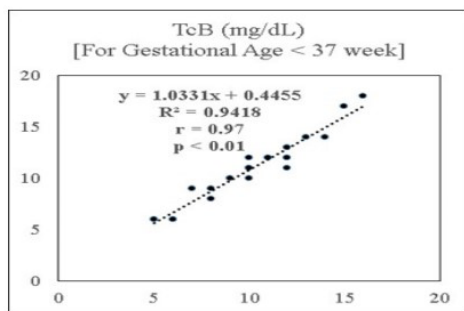


Figure 3: TSB versus TcB measurements in neonates less than 37 weeks of gestation

From figure 3, we observed highly significant correlation $r = 0.97$ ($p < 0.01$) between TcB and TSB in neonates of gestational age less than 37 weeks (preterm neonates).

Table 3: Frequency and percentage of serum bilirubin versus cutaneous bilirubin

TcB (mg/dl)	TSB (mg/dl)		Total
	Abnormal	Normal	
Abnormal	81	15	96
Normal	1	65	66
Total	82	80	162

Table 3 showed the frequency and percentage of serum bilirubin as compared with cutaneous bilirubin in normal and abnormal states for calculating positive and negative predictive values of cutaneous bilirubin based on serum bilirubin. In this table, bilirubin levels below 12 were considered normal.

In this study the positive and negative predictive values of TcB were 84.4% and 98.5% whereas sensitivity and specificity were 98.8% and 81.3% respectively.

DISCUSSION

Jaundice is one of the most prevalent clinical problems during neonatal period which requires interventional treatment.¹¹ Most icteric neonates do not have any other disorders but due to toxic effects of bilirubin on neural cells, it may lead to kernicterus which is a chronic, degenerative and debilitating disease.¹²

Measuring the serum bilirubin level is one of the most common laboratory tests carried out in neonates. This test is painful and can cause increased risk of sepsis on them. Also, this test is stressful to both the neonate and parents and it also requires a lot of time and money. Therefore, a reduction in repeated blood sampling is very important and it might be achieved by utilizing and setting the new set of tools that are available in market, for cutaneous measurement of bilirubin concentration. Different studies have been done to evaluate the sensitivity and accuracy of these tools, according to which different results have been obtained.¹³⁻¹⁵

Out of 162 neonates, 100(61.7%) of them were male and 62(38.3%) were female i.e. male to female ratio of 1.6:1. Similar finding was there in a study done by Mansouri M et al.¹⁶ which showed male to female ratio of 1.63:1. In a study conducted by Gondale G et al.¹⁷, male to female ratio was 1.2:1. A study done by Saeed T et al.¹⁸ among 122 neonates reported jaundice among 66 males and 56 females i.e. male to female ratio of 1.2:1. The reason behind this could be due to the fact that parents are more anxious and are of more health seeking behavior when it comes to be for a male child as compared to female child which is common in Indian subcontinent.

In this study, 130(80.2%) neonates were between 2.5 – 4 kg birth weight. 28(17.3%) neonates were below 2.5 kg i.e. low birth weight. Similar results were found on a study performed by Mishra S and et al.¹⁹ where neonates with birth weight 2.5-4 kg were 87.5% and less than 2.5 kg were 4%. A study conducted by Dhanjal G S et al.²⁰ also consisted of 74% neonates of birth weight more than 2.5 kg and 23% between 1.5-2.5 kg birth weight. Above results suggests that there is significant hyperbilirubinemia in preterm neonates but result found to be less as the total number of preterm neonates were less in those studies. Low birth weight has been taken as one of the risk factor for neonatal hyperbilirubinemia by AAP guidelines.⁵ Delay in enteral feeding in sick low birth weight babies may cause delay in colonization of gastrointestinal tract leading to enhancement of bilirubin enterohepatic circulation and causing hyperbilirubinaemia.

In the current study, a high correlation between TcB and TSB measurements in neonates ($r = 0.981$) was found with p value < 0.0001). In a study performed by Mansouri M et al.¹⁶, a high correlation ($r=0.89$) was observed between TSB and TcB. Similarly, a study conducted by Gupta B.K et al.²¹ also showed significant correlation between TcB and TSB. In a prospective correlation study performed by Lam SK et al.²², transcutaneous bilirubin showed a good correlation with total serum bilirubin. A strong correlation between plasma and transcutaneous

bilirubin assays was observed in a cross-sectional study done by Povaluk P et al.²³ Similar findings were observed in study conducted by Leite M et al.¹³ and Mahram M et al.²⁴ So, several studies have been done in this regard and have shown high correlation between TcB and TSB measurements in neonates. Some minor differences in the mentioned studies could be due to differences in the type of bilirubinometers, skin color, ethnicity, individual variability, laboratory methods and kits.

23 (14.2%) preterm neonates defined by neonates less than 37 weeks of gestation and 139 (85.8%) terms (37-42 weeks of gestation) were included in this study. With respect to the effects of gestational age on the correlation between TcB and TSB, correlation coefficient of 0.98 and 0.97 in term and preterm respectively was found which suggested strong correlation between TcB and TSB in both groups of neonates. Hun H J et al.²⁵ found an excellent correlation between TcB and TSB in term neonates ($r = 0.82$, $p < 0.01$) as well as in premature ones ($r = 0.81$, $p < 0.01$). Douville et al.²⁶ also found an excellent correlation between TcB and TSB in term neonates as compared with premature ones

The study may not be entirely representative of the whole neonatal population of Nepal, as it is a hospital-based study

done on a small sample size and carried out only in one institution over a short duration of time. The bilirubinometer also could not measure high bilirubin level, so it is in apparent for those cases.

CONCLUSION

There was a high correlation between TcB and TSB level in neonates ($r = 0.981$) and this finding was statistically significant (p value < 0.001). The sensitivity and specificity of cutaneous bilirubin were 98.8% and 81.3% respectively. Correlation coefficient of 0.98 and 0.97 were found in term and preterm neonates respectively, which suggested strong correlation between TcB and TSB in both groups of neonates. Due to its simplicity and painlessness, serial cutaneous bilirubin measurements would be helpful in following neonatal icterus. Although TcB has a high sensitivity in detecting icterus, it should not replace TSB due to its relatively low specificity. Therefore, in high risk neonates, measuring TSB alongside TcB is necessary.

CONFLICT OF INTEREST: None

FINANCIAL DISCLOSURE: None

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