ORIGINAL ARTICLE

MEAN DIFFERENCE BETWEEN TRANSCUTANEOUS AND SERUM BILIRUBIN MEASUREMENTS

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ABSTRACT

Background: Total Serum bilirubin (TSB) is considered as the most authentic method for determining bilirubin levels. However, Transcutaneous Bilirubinometer, uses photometry to detect bilirubin level and can be considered as a reliable tool to assess bilirubin for the screening of neonatal jaundice in term neonates

Objective: To determine the mean difference between Transcutaneous bilirubin and serum bilirubin among jaundiced neonates.

Methods: This cross sectional study was conducted at Neonatal Intensive unit, Ziauddin University Hospital, Karachi. Total 150 patients, with clinical jaundice were included. Transcutaneous measurements were taken by application of Drager JM-105 (transcutaneous bilirubinometer) to the sternum of infants. Three readings were taken and the average value was recorded. Blood samples were obtained and Serum bilirubin was estimated. The difference of bilirubin in TcB and TSB techniques was calculated and compared using student t-test. Descriptive statistics were also calculated. Stratification was done and poststratification again student t-test was applied. P-value ≤0.05 was taken as significant in all analysis.

Results: There were 78.7% male and 21.3% female patients. Mean age was 4.50±3.19 days. Mean weight of neonates was 2253.93±533.59 grams. Mean gestational age was 36.14±1.04 weeks. Mean bilirubin level in TcB and TSB was 13.04±4.07 mg/dl and 12.79±5.49 mg/dl respectively. The difference of bilirubin in TSB and TCB was -0.246±2.53 mg/dl and was not significant.

Conclusion: There was no significant mean difference of bilirubin in TCB and TSB techniques, therefore, Transcutaneous bilirubinometery can be accepted as a good device for the screening of neonatal jaundice.

Keywords: Difference, Transcutaneous Bilirubin, Serum Bilirubin, Jaundice, Neonates

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INTRODUCTION

One of the most common problems during neonatal age is jaundice;[1] especially in Asia.[2] Serious complications of jaundice in neonates include transient encephalopathy and kernicterus for which bilirubin measurements are extremely crucial for early detection.[3] For this reason, unit of the American Academy of Pediatrics committee on Hyperbilirubinemia advocated for the screening of all neonates before sending them home[4,5]. Bilirubin levels can be assessed via visual method but this method is imprecise, requires clinical expertise and is affected by light and clothes [3]

Serum bilirubin (TSB) is the most reliable method for determining bilirubin levels but this is an invasive method, can cause infections, is stressful and agonizing for the neonate and immediate results are not received.[4,6,2] Thus, a noninvasive technique was devised to determine bilirubin level, via transcutaneous bilirubinometer, that uses photometry to detect bilirubin level.[2] The first transcutaneous bilirubinometer was introduced in the 1980s and it determined bilirubin level through the intensity of yellow discolouration.[1]

Numerous studies done internationally since then have established the efficacy of this device and proved it to be a good screening tool. The study done by Mansouri calculated correlation between the two methods[3]. Mahram and Oveisi concluded that TcB can be considered as a reliable tool to evaluate bilirubin for the screening of neonatal jaundice in term neonates.[6]

Taylor et al. concluded that variance between TcB and TSB levels were enhanced in African-American newborns and varied based on brand of meter used.[4] They also found out that 2.2% of TcB measurements underrated the (TSB) by 3.0 mg/dL, and the chances for TcB to underestimate TSB increased with progressive newborn age4. Maisels and Bosschaart aforesaid that TcB cannot replace TSB because 99% of what TCB assess is the extravascular tissue bilirubin and not in the blood.[5,7,8]

Some small-scale studies have been done locally. A study done in AKUH in 1991 by Bhuttaet et al. displayed a high correlation in the results but it was performed on a small population.[9] Lately, a study done in Rawalpindi by Saeed and Zahoor ul Haq found TcB a screening device, which offers an accurate, rapid, economic and noninvasive means of assessing plasma bilirubin concentrations in neonates. Since there is scarcity of data regarding the mean difference between TSB and TcB levels so a pilot study was conducted. This showed mean and standard deviation of -0.13+/-2.5.10
Since, locally, limited studies have been done and the data on the mean difference of two techniques is also not available. Once the reliability of TcB is established, the neonates can be saved from the noxious effects of pricks and a speedy, economical method can be established to assess bilirubin levels. The objective of this study was to compare the mean difference between Transcutaneous bilirubin and serum bilirubin among jaundiced patients.

METHODS

This cross sectional study was conducted at Neonatal Intensive unit of Ziauddin University Hospital, Karachi, from May to November 2018. The non-probability consecutive sampling was used as a sampling technique. The sample size was calculated using WHO sample size calculator taking mean difference between TcB and TSB= -0.13±2.59 (from our pilot study results), confidence interval 95% and margin of error 0.01.

Total 150 neonates between 1 to 28 days of age of either gender with clinical jaundice (Visible yellowish discoloration on the skin), Hyperbilirubinemia (total serum bilirubin level above 5 mg/dl) were included in the study. Neonates who were exposed to Phototherapy were not included. Ethical approval was obtained from institutional ethical committee and an informed consent was also taken from parents or the caretaker of the patient.

Total Serum bilirubin (TSB) present in the blood was measured by blood sampling. Transcutaneous bilirubin (TcB) was measured via transcutaneous bilirubinometer which is a portable, hand held, rechargeable device that assessed the level of bilirubin by non-invasive method. The mean difference between TSB and TcB was calculated. Demographic information was obtained from the parents/ guardians like age and gender. Transcutaneous measurements were taken by application of Drager JM-105 (transcutaneous bilirubinometer) to the sternum of infants. Three readings were taken and the average value was recorded. Blood samples were obtained from a peripheral vein under strict aseptic conditions within 10 minutes of transcutaneous bilirubin measurements. Serum bilirubin was estimated by Jandrassik method on Roche Hitachi 902 automated chemistry analyzer. The results of bilirubin level for both the techniques were compared and difference was recorded.

By using SPSS, data were compiled and analyzed. Descriptive statistics were calculated. Mean and standard deviation were calculated for quantitative variables like age, gestational age, weight, TSB, TcB and difference of TSB & TcB. For qualitative variables like gender and blood group of neonate and mother, frequency and percentages were calculated. The mean difference of bilirubin level in TcB and TSB was compared using student t test. Effect modifiers like age, gestational age, weight, gender, blood groups of baby and mother were controlled through stratification. Post stratification t-test was applied keeping P value ≤ 0.05 as significant.

RESULTS

The mean age of neonates was 4.50±3.19 days. The mean weight was 2253.93±533.59 grams. The mean gestational age was 36.14±1.04 weeks. The mean Transcutaneous bilirubin (TcB) and Total Serum bilirubin (TSB) were 13.04±4.07 mg/dl and 12.79±5.49 mg/dl, respectively. The mean difference of bilirubin level of TSB and TcB were -0.246±2.53 mg/dl.

The detailed descriptive statistics are presented in Table 1.

Table 1: Descriptive statistics of age, weight, gestational age, TcB, TSB, and difference of TcB & TSB.

(n=150)	Mean±SD	Median	Range	Minimum	Maximum
Age (days)	4.50±3.19	3.00	17	1	18
Weight (grams)	2253±533.29	2200	2340	1260	3600
Gestational Age (weeks)	36.14±1.04	36.00	5	35	40
TcB (mg/dl)	13.04±4.07	12.05	14.10	5.40	19.50
TSB (mg/dl)	12.79±5.49	12.74	18.83	5.97	24.80
Difference (TcB-TSB)	-0.246±2.53	-0.430	11.76	-4.96	6.80

The male neonates were 78.7% and female, 21.3%. The age, weight, and gestational age were further stratified in groups. The frequency and percentages of neonates according to stratified groups were also calculated. The detailed results are presented in Table 2.

Table 2: Frequency distribution of gender and stratified groups of age, weight, and gestational age

(n=150)	Study Group	Frequency (n)	Percentage (%)
Gender	Male	118	78.7
	Female	32	21.3
Age Group	≤7 days	127	85.0
	>7 days	23	15.0
Gestational Age	≤36 weeks	125	83.0
	> 36 weeks	25	17.0
Weight	<2500 grams	98	65.0
	≥2500 grams	52	35.0

As far as blood groups are concerned, most common blood groups were A^{+ve} and O^{+ve} among neonates and their mothers. The frequencies are presented in Figures 1 and 2.

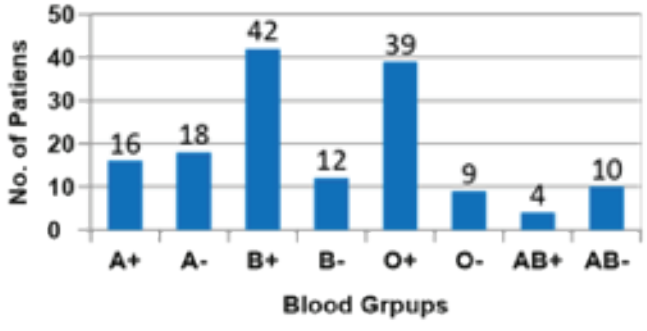

Figure 1: Frequency distribution of Mother's Blood Groups.

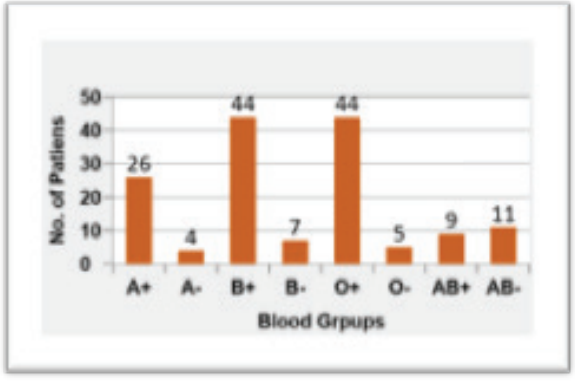

Figure 2: Frequency distribution of Neonates Blood Groups.

Stratification with respect to gender, age, weight, gestational age, mother's blood group and neonate's blood group was done to compare mean difference of bilirubin level among TcB and TSB. P-value ≤0.05 was considered as significant. The results showed that there is no significant mean difference between in bilirubin level calculated by TSB and TcB (p=0.237). Mean comparison of bilirubin level in TcB and TSB technique was also done for groups of gender, age, weight, gestational age, mother's blood group and neonate's blood. The detailed results of comparisons are presented in Table 3.

Table 3: Comparison of mean bilirubin level among TSB and TcB.

Total (n=150)		TcB		TSB		P-value
		Mean	SD	Mean	SD	
		13.04	4.07	12.79	5.49	0.237**
Gender	Male	12.74	4.14	12.49	5.60	0.288**
	Female	14.11	3.65	13.91	4.97	0.611**
Age	≤ 7 days	13.09	4.01	12.90	5.49	0.409**
	>7 days	12.74	4.45	12.17	5.59	0.291**
Gestational Age	≤ 36 weeks	13.13	3.84	12.84	5.26	0.190**
	> 36 weeks	12.55	5.15	12.53	6.62	0.974**
Weight	<2500 grams	13.19	3.91	12.85	5.42	0.192**
	≥2500 grams	12.74	4.39	12.67	5.67	0.844**
Mothers Blood Groups	A +ve	11.80	4.07	11.27	4.60	0.170**
	A -ve	13.58	4.52	13.27	5.57	0.523**
	B +ve	13.83	4.03	13.76	5.68	0.888**
	B -ve	13.51	3.84	12.94	5.84	0.537**
	O +ve	12.54	3.76	12.27	5.58	0.551**
	O -ve	13.75	4.89	14.67	6.82	0.366**
	AB +ve	12.20	2.09	11.59	4.28	0.639**
	AB -ve	11.78	4.85	10.92	4.34	0.058**
Neonates Blood Groups	A +ve	13.17	4.16	12.97	5.63	0.707**
	A -ve	12.15	4.38	11.60	5.78	0.565**
	B +ve	13.47	3.98	13.32	5.38	0.692**
	B -ve	9.66	2.90	8.29	3.22	0.239**
	O +ve	13.34	3.94	13.32	5.59	0.967**
	O -ve	11.12	2.15	8.91	3.72	0.216**
	AB +ve	9.93	3.66	9.15	4.41	0.109**
	AB -ve	15.65	4.23	16.16	4.95	0.441**

*Student t Test was applied ** Not significant at 0.05 levels*

DISCUSSION

For early detection of hyperbilirubinemia, TcB screening is a reliable technique because of its rapidity and non invasiveness.[11] Several readings can be taken on a neonate effortlessly. Additionally, instant results are provided compared to serum bilirubin levels, which is time consuming.[4] With the availability of TcB as an early screening device for hyperbilirubinemia, the process of early detection can be made more economical.[12]

Many researchers previously concluded that there was good correlation between TSB and TcB levels coefficients (0.77-0.97)13-15. Factors that increased the precision included regular monitoring of device and TcB measurement training.[16]

Kernicterus is the major complication with raised and undetected hyperbilirubinemia, which needs to be prevented. For this reason, expert committees have advised screening in all newborns for jaundice.[11]

The importance of TcB is evident from a study done by a neonatal committee to find out the topics prioritized by its members for research. TcB, as a screening tool for jaundice, was declared as one of the pivotal subject for experimentation.[17] In another study, babies of diverse races were evaluated for jaundice with various devices. TcB measurement

revealed precise approximation of TSB values. Grossly, this concluded that TcB measurements can be fairly relied upon.[4]

An important concern with TcB screening is that it provided less precise approximation of TSB values at higher TSB levels. Whereas, with lower levels, TcB overrated TSB values. One study showed that with TSB levels of > 15 mg/dl, respective TcB was 1.4 mg/dl lower than TSB levels.

Engle et al.[13] also found that TcB measurements underestimated TSB at higher levels. Similarly, in one of the few assessments of TcB use in newborns, the overall correlation between TcB and TSB levels was 0.77, with increasing variability at higher TSB values4. One research shows that there are no significant differences in the accuracy of TcB measurement based on anatomic site used for the assessment (either forehead or chest). Nevertheless, in nurseries that used both anatomic sites for measurement, TcB–TSB differences were significantly raised. This may suggest that accuracy is maximized when the procedures for TcB measurement are standardized according to site, regardless of the specific site chosen.[4]

A previous study showed greater variation between TcB and TSB measurements with the advancing age of the baby. The results were not clearly explained but the researchers concluded that the changes occurring in a baby such as the hemoglobin concentration, may bring about such results.[21]

Rodríguez-Capote et al. assessed the association between TCB measurements, performed using Bili-Check or Minolta Air-Shields JM-103, and TSB and evaluated the predictive accuracy of TCB measurements for risk using the nomogram. They found that both devices had a good correlation with the laboratory method, but underestimated the serum bilirubin. In that study, after correcting for the differences using either the bias or the 95% CI the false negative rate was reduced to zero in all cases. They concluded that TCB measurements cannot be directly applied to a TSB nomogram but must be adjusted for any observed biases to avoid misclassifying newborns at risk for hyperbilirubinemia.[22] Similarly, Wainer et al. and Sajjadian et al. found the same underestimation in their study.[23,24] Some researchers also found higher levels of bilirubin through TCB than TSB. The result of their study revealed that TCB and TSB values had a linear correlation with a significant correlation coefficient (r 0.81, P<0.001).[25]

Some difference could be seen in values of TCB comparing TSB. TCB in some studies was found higher and in some lower than TSB. The reason may be due to some factors such as difference in devices of transcutaneous bilirubinometery, difference in skin darkness of cases, probably including cases with hemolytic jaundice in some studies (showing TSB levels higher than TCB because the rate of bilirubin production in serum is higher and earlier than the time skin becomes icteric), and probability of including some cases who had received phototherapy before assessments cannot be ruled out.[26]

This study had some limitations. The study was a single hospital-based study with a small sample size, and conducted in urban environment, therefore, the results might not be generalizable to larger populations. More studies with bigger sample size are required.

CONCLUSION

This study showed mean bilirubin level of TcB and TSB was 12.79±4.54 mg/dl and 12.67±5.66 mg/dl, respectively. The mean difference of bilirubin level among two techniques was -0.126±2.55 mg/dl and which was also insignificant. This concluded that transcutaneous bilirubinometery can be accepted as a good device and a reliable tool to assess bilirubin (hyperbilirubinemia) for the screening of neonatal jaundice to reduce repeated blood sampling.

REFERENCES

1.Povaluk P, Shwetz EA, Kliemann R. Comparative study between plasma and transcutaneous bilirubin measurements in newborns. Revista Paulista de Pediatria 2011; 29(1):6-12.
2.Radfar M, Hashemieh M, Shirvani F. Transcutaneous bilirubinometry in preterm and term newborn infants before and during phototherapy. Arch Iranian Med 2016;19(5):323.
3.Mansouri M, Mahmoodnejad A, Taghizadeh SR, Gharibi F. A comparison between transcutaneous bilirubin (TcB) and total serum bilirubin (TSB) measurements in term neonates. Int J Pediat 2015;3(3.1):633-41.
4.Taylor JA, Burgos AE, Flaherman V, Chung EK, Simpson EA, Goyal NK, et al. Discrepancies between transcutaneous and serum bilirubin measurements. Pediatrics 2015;135(2):224-31.
5.Maisels MJ. Transcutaneous bilirubin measurement: does it work in the real world? Pediatrics 2015;135(2):364-6.
6.Mahram M, Oveisi S, Jaberi N. Transcutaneous bilirubinometery versus serum bilirubin in neonatal jaundice. Acta Medica Iranica 2015;53(12):764-9.
7.Bosschaart N, Kok JH, Newsum AM, Ouweneel DM, Mentink R, van Leeuwen TG, et al. Limitations and opportunities of transcutaneous bilirubin measurements. Pediatrics 2012;129(4):689-94.
8.Karen T, Bucher HU, Fauchère JC. Comparison of a new transcutaneous bilirubinometer (Bilimed®) with serum bilirubin measurements in preterm and full-term infants. Bio Med Cect Pediatr 2009;9(1):1.
9.Bhutta ZA, Yusuf KA. Transcutaneous

bilirubinometry in Pakistani newborns: a preliminary report. J Pak Med Assoc 1991;41:155-6.
10.Saeed T, UlHaq MZ, Butt M, Raja TM, Zulfiqar R. Validity of transcutaneous bilirubinometer in neonates as compared to laboratory serum bilirubin estimation. J Rawalpindi Med Col (JRMC) 2013;17(1):81-3.
11.Maisels MJ, Bhutani VK, Bogen D, Newman TB, Stark AR, Watchko JF. Hyperbilirubinemia in the newborn infant > or =35 weeks' gestation: an update with clarifications. Pediatrics 2009;124(4):1193–8.
12.Maisels MJ, Kring E. Transcutaneous bilirubinometry decreases the need for serum bilirubin measurements and saves money. Pediatrics 1997;99(4):599–601.
13.Engle WD, Jackson GL, Sendelbach D, Manning D, Frawley W. Assessment of a transcutaneous device in the evaluation of neonatal hyperbilirubinemia in a primarily Hispanic population. Pediatrics 2002;110:61–7.
14.Ebbesen F, Rasmussen LM, Wimberley PD. A new transcutaneous bilirubinometer, BiliChek, used in the neonatal intensive care unit and the maternity ward. Acta Paediatr 2002;91:203–11.
15.Grohmann K, Roser M, Rolinski B. Bilirubin measurement for neonates: comparison of 9 frequently used methods. Pediatrics 2006;117(4):1174–83.
16.Maisels MJ. Historical perspectives: transcutaneous bilirubinometry. Neoreviews 2006;7(5):217–25.
17.Simpson E, Goyal NK, Dhepyasuwan N. Prioritizing a research agenda: a Delphi study of the Better Outcomes through Research for Newborns (BORN) network. Hosp Pediatr 2014;4(4):195–202.
18.Maisels MJ, Ostrea EM Jr, Touch S, Clune SE, Cepeda E, Kring E, et al. Evaluation of a new transcutaneous bilirubinometer. Pediatrics 2004;113:1628 –35.
19.Engle WD, Jackson GL, Stehel EK, Sendelbach DM, Manning MD. Evaluation of a transcutaneous jaundice meter following hospital discharge in term and near-term neonates. J Perinatol 2005;25(7):486–90.
20.Yamauchi Y, Yamanouchi I. Transcutaneous bilirubinometry: effect of postnatal age. Acta Paediatr Jpn1991;33(5):663–7.
21.Jopling J, Henry E, Wiedmeier SE, Christensen RD. Reference ranges for hematocrit and blood hemoglobin concentration during the neonatal period: data from a multihospital healthcare system. Pediatrics 2009;123(2): e333-7.
22.Rodrı´guez-Capote K, Kim K, Paes B, Turner D, Grey V. Clinical implication of the difference between transcutaneous bilirubinometry and total serum bilirubin for the classification of newborns at risk of hyperbilirubinemia. Clin Biochem 2009;42:176–9.
23.Wainer S, Parmar SM, Allegro D. Impact of a Transcutaneous Bilirubinometry Program on Resource Utilization and Severe Hyperbilirubinemia. Paediatrics 2012;129(1):77-86.
24.Sajjadian N, Shirazi H, Saalehi Z. Transcutaneous Bilirubin Measurement in Preterm Neonates. Acta Med Iran 2012;50(11):765-70.
25.Panburana J, Boonkasidach S, Rearkyai S. Accuracy of transcutaneous bilirubinometry compare to total serum bilirubin measurement. J Med Assoc Thai 2010;93(Suppl2):81-6.
26.Amoozgar H, Rastegar M. Making a transcutaneous icterometer in Neonates. Iran J Pediatr 2007;17(Suppl12):224-30.