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The Forehead is a Better Site than the Sternum to Check Transcutaneous Bilirubin during Phototherapy in Neonate

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ABSTRACT

Background: Total serum bilirubin (TSB) testing is typically necessary for the management of jaundiced neonates; in infants not undergoing phototherapy, transcutaneous bilirubin (TCB) was more accurate. It is preferable to evaluate TCB at the forehead during phototherapy as opposed to the sternum.

Objectives: This study aimed to confirm the accuracy of TCB in the neonatal intensive care under phototherapy and compare forehead and sternum as the TCB assessment site.

Patients and methods: A Prospective observational study was conducted on 88 Neonates under phototherapy conducted at the NICU of Menoufia University Hospital and AL Helal Insurance Hospital, during the period from august 2022 to September 2023.

Results: ROC curve analysis showed that cutoff point of TSB in neonates with hyperbilirubinemia was 9.85 mg/dl, with sensitivity of 87.7%, specificity of 27.3% at AUC of 0.743, cutoff point of TCB forehead for detection of jaundice in neonates with hyperbilirubinemia was 7.350 mg/dl, with sensitivity of 84.6%, specificity of 90.9% at AUC of 0.628 and cutoff point of TCB sternum for detection of jaundice in neonates with hyperbilirubinemia was 3.70mg/dl, with sensitivity of 74.3%, specificity of 81.8% at AUC of 0.608

Conclusion: The variations in skin composition that have been noticed in the TCB measurements at the forehead and sternum may be the cause of the variances in TCB estimate. This is because the concentration of collagen and melanin can alter the wavelength that TCB photometry detects.

Keywords: Bilirubin, Jaundice, Neonate, Phototherapy, Transcutaneous.

INTRODUCTION

The blood's buildup of bilirubin is what causes jaundice. It may be brought on by either an excess of bilirubin or an inability to metabolise and eliminate it. About 1 in 2500 to 5000 live babies have infantile jaundice, which can have a range of underlying illnesses, from mild jaundice from breast milk to severe, potentially fatal conditions such as liver failure and biliary atresia (BA). While some illnesses have clear clinical characteristics, others may present more subtly, requiring a high index of suspicion to make the diagnosis [1].

The most prevalent ailment among neonates that needs medical treatment and a readmission to the hospital is jaundice. Unconjugated bilirubin builds up in neonates with jaundice, causing the skin and sclera to become yellow. Unconjugated hyperbilirubinemia in most babies is a typical transitory condition. Serum bilirubin levels, however, can rise abnormally in certain neonates, which can be concerning because unconjugated bilirubin is neurotoxic and can result in neonatal mortality as well as lasting neurologic consequences in those who survive (kernicterus). For these reasons, a diagnostic assessment is often prompted when newborn jaundice is present [2]. Before neonates are discharged from the hospital, the American Academy of Paediatrics (AAP) advises screening for jaundice and related risk factors. Transcutaneous bilirubin (TCB) evaluation has been used extensively for screening in healthy babies since it doesn't involve blood collection and yields results quickly. In contrast, blood collection is necessary for TSB evaluation, which is a painful and intrusive process [3].

A larger number of studies have found that TCB is an accurate and suitable substitute for TSB in preterm newborns, despite some reports suggesting that TCB is less reliable in preterm infants than in full-term infants [4]. The evaluation of TCB has been extended to newborns undergoing phototherapy. Regarding the precision and application of TCB during phototherapy, several recent findings have been published [5].

The gold standard for determining hyperbilirubinemia is TSB estimation; however, it is an invasive procedure that necessitates blood collection and is inconvenient due to venous puncture technical difficulties, pain, discomfort, delayed results, and parental anxiety. As such, it is crucial to minimise the amount of blood lost by the newborn during blood draws and to minimise the number of draws [6].

The aim of this study was to confirm the accuracy of TCB in the NIC under phototherapy and compare forehead and sternum as the TCB assessment site.

PATIENTS AND METHODS

A Prospective observational study that was conducted on 88 neonates under phototherapy conducted at the Neonatal Intensive Care Unit (NICU) of Menoufia University Hospital and AL Helal Insurance Hospital .

Inclusion criteria: Neonates in NICU under phototherapy.

Exclusion criteria: Neonates not under phototherapy**,** neonates with a condition that could interfere with TCB measurements, such as congenital anomalies of forehead and sternum, hydrops fetalis, edema, diffuse

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cutaneous conditions, infection, or purpura and direct hyperbilirubinemia.

Every neonate enrolled in the research underwent the following:

Medical history: Family history of consanguinity and similar attacks, maternal history of previous abortion, blood transfusion infection, drug intake during pregnancy, gestational age (The GA of the neonates were determined by last menstrual period if known, by antenatal ultrasonography or by Ballard method), perinatal history (mode of delivery, birth trauma, gestational age, birth weight, gender and drug intake), postnatal history and time of appearance of jaundice (onset).

Clinical examination: A general and systemic examination was done, with a focus on vital signs, anthropometric measurements, the existence of cerebral haemorrhage, and neurological evaluation.

Laboratory investigations: Complete blood count and retics: 2 ml of blood on EDTA tube by Advia 2120 apparatus, which use laser light scatter technology for determination of blood count and platelet count, Coombs test, TSB and DSB (Using AU480 Beckman apparatus), blood group, Rh and Liver enzymes (Using AU480 Beckman apparatus)**.**

The TSB and TCB were measured at the forehead and sternum using a bilirubinometer (Being MBJ30 and Drager JM-105). We investigated the relationship between the TSB and TCB measurements at the forehead and sternum during phototherapy.

Ethical approval: Medical Ethics Committee of Faculty of Medicine, Menoufia University gave its approval to this study. Signed informed permissions from parents of neonates following an explanation of the study's purpose. The Helsinki Declaration was followed throughout the study's conduct.

Statistical Analysis

With SPSS V. 25.0, the results were statistically evaluated. We utilised the Shapiro-Walk test to determine if the data were normally distributed. Frequencies and relative percentages are used to represent qualitative data. χ^2 test was used to compare the differences between two or more sets of qualitative variables. The statistical information was presented as mean ± SD. Additionally, the ROC analysis was used for the case-specific marker prediction level. A significant level is defined as P-values ≤ 0.05.

RESULTS

A total of 88 neonates who had jaundice were included in our study, their gestational ages ranged from 34-39 weeks with a mean of 37.44 ± 0.90. 50 (56.8%) of them were males and 38 (43.2%) were females. Also, 65 (73.9%) neonates their delivery was Cesarean section and 23 (26.1%) their delivery was normal vaginal. 2nd day was the most time of appearance of jaundice (34.1%) (Table 1).

Table (1): Demographic characteristics of the studied patients (N=88).

Variables	The studied patients (n=88)	
	Mean ±SD	**Range**
Gestational age/weeks	37.44±0.90	34.00-39.00
Birth (weight/Kg)	3.52±0.39	2.90-4.50
	No.	**%**
Sex		
Male	50	56.8
Female	38	43.2
Mode of delivery		
CS	65	73.9
NVD	23	26.1
Time of appearance onset		
1st day	7	8.0
2nd day	30	34.1
3rd day	23	26.1
4th day	20	22.7
5th day	8	9.1

CS: Cesarean section, NVD: Normal vaginal delivery

Among 88 neonates, 9 (56.8%) of them were positive consanguinity. Previous sibling with hyperbilirubinemia were found in 35 (39.4%). Moreover, there were 26 neonates who had maternal disease, 7 patients (8.0%) had hypertension and bleeding placenta previa followed by 6 (6.8%) patients had common cold last week of pregnancy, 4 (4.5%) had maternal contraction, and 1 patient (1.1%) had Prom and anemia (Table 2).

Table (2): Family history and Maternal history among the studied cases (n=88).

	Variables	The studied Cases (n=88)	
		No.	**%**
Consanguinity	Negative	79	89.8
	Positive	9	10.2
Sibling	1st	28	31.8
	2nd	26	29.5
	3rd	32	36.4
	4th	2	2.3
Similar disease	No (other sibling)	53	60.2
	Yes (other sibling)	17	19.3
	Yes (1st sibling)	9	10.2
	No similar disease	8	9.1
	Other 2 sibling admitted	1	1.1
Maternal disease	No	26	29.5
	HTN	7	8.0
	Bleeding placenta previa	7	8.0
	PROM	1	1.1
	Anemia	1	1.1
	Common cold last	6	6.8
	week of pregnancy	4	4.5
	Maternal contraction		

DM: Diabetes mellitus **HTN:** Hypertension **UTI:** Urinary tract infection **TTN:** Transient tachypnea of the newborn **PDA:** Patent ductus arteriosus **Prom:** Premature rupture of membranes.

Lab investigation indicated that mean TLC was 11.89 ± 2.86, Hb was 14.53 ± 2.24, PLT was 298.67 ± 73.88, Retics was 5.87 ± 1.41, AST was 31.75 ± 7.76p, ALT was 21.38 ± 5.21, TSB was 12.12 ± 2.46, DSB was 0.92 ± 0.22, Forehead TCB was 11.08 ± 2.69 and Sternum TCB was 6.82 ± 1.68). 4 (4.5%) patients were positive Coombs's test. Moreover, the most blood group of mothers was O (+ve) (60.2%), and the most blood group of babies was B (+ve) (70.5%) (Table 3).

Table (3): Lab investigation among the studied cases (N=88).

Variables	The studied Cases (n=88)	
	Mean ± SD	
TLC (10^3/mm^3)	11.89 ± 2.86	
Hb (g/dL)	14.53 ± 2.24	
PLT (x10^9/L)	298.67 ± 73.88	
Retics	5.87 ± 1.41	
AST (U/L)	31.75 ± 7.76	
ALT (U/L)	21.38 ± 5.21	
TSB (µmol/L)	12.12 ± 2.46	
DSB (µmol/L)	0.92 ± 0.22	
Forehead TCB (µmol/L)	11.08 ± 2.69	
Sternum TCB (µmol/L)	6.82 ± 1.68	
	No.	**%**
Coombs's test		
Negative	77	87.5
Positive	11	12.5
ABO		
Mother Blood group		
O (+ve)	53	60.2
A (+ve)	8	9.1
B (+ve)	13	14.8
A (-ve)	7	8.0
AB (+ve)	7	8.0
Babies blood group		
A (-ve)	7	8.0
A (+ve)	16	18.2
B (+ve)	62	70.5
AB (+ve)	1	1.1
B	1	1.1
Rh		
Negative	0	0.00
Positive	88	100.0

TLC: u, Hb: Hemoglobin, **PLT**: platelet, **AST**: aspartate aminotransferase, **ALT**: alanine transaminase, **TSB:** Total serum bilirubin, **DSB:** Direct serum bilirubin, **TCB:** Transcutaneous bilirubinometer, **Rh:** Rhesus factor **ABO:** Blood group system.

There was significant difference regarding TSB - TCB forehead, TSB- TCB sternum and TCB forehead- TCB sternum with means of 1.04 ± 2.72, 5.30 ± 2.85 and 4.27 ± 1.86, (P<0.05) respectively. Moreover, TSB's mean was significantly higher than the mean of TCB measured at the forehead (P = 0.001) and sternum (P<0.001) (Table 4).

Table (4): Multiple pairwise comparisons of TSB, sternum, and forehead TCB.

Variables	Paired Differences				
	Mean ±SD Diff.	95% CI		*t*	*P-value*
		Lower	Upper		
TSB - TCB Forehead	1.04±2.72	0.46	1.61	3.573	**0.001***
TSB - TCB Sternum	5.30±2.85	4.70	5.91	17.452	**<0.001***
DSB - TCB Forehead	-10.17±2.64	-10.73	-9.61	36.081	**<0.001***
DSB - TCB Sternum	-5.90±2.64	-6.46	-5.34	20.994	**<0.001***
TCB Forehead- TCB Sternum	4.27±1.86	3.87	4.66	21.542	**<0.001***

TSB: Total serum bilirubin **TCB:** Transcutaneous bilirubinometer **t:** student t test **CI:** Confidence Interval.

ROC curve analysis showed that cutoff point of TSB in neonates with hyperbilirubinemia was 9.85, with sensitivity of 87.7%, specificity of 27.3% at AUC of 0.743, cutoff point of TCB forehead for detection of jaundice in neonates with hyperbilirubinemia was 7.350, with sensitivity of 84.6%, specificity of 90.9% at AUC of 0.628 and cutoff point of TCB sternum for detection of jaundice in neonates with hyperbilirubinemia was 3.70, with sensitivity of 74.3%, specificity of 81.8% at AUC of 0.608 (Table 5 and figures 1-4).

Table (5): ROC curve of TSB and DSB in neonates with hyperbilirubinemia and TCB forehead and TCB sternum for detection of jaundice.

							95% CI	
Test Result Variable (s)	**Area**	**Std. Error**	**Sig.**	**Sens.**	**Spec.**	**Cutoff value ≥ a**	**Lower**	**Upper**
TSB	0.743	0.075	**0.01***	85.7	27.3	9.85	0.60	0.89
DSB	0.745	0.102	**0.009***	93.5	27.3	0.530	0.54	0.94
TCB Forehead	0.628	0.080	0.171	89.6	90.9	7.350	0.47	0.78
TCB Sternum	0.608	0.085	0.248	88.3	81.8	3.70	0.44	0.78

TSB: Total serum bilirubin**, Sens.:** Sensitivity **Spec.:** Specificity **CI:** Confidence Interval, **TCB:** Transcutaneous bilirubinometer, **DSB:** Direct serum bilirubin

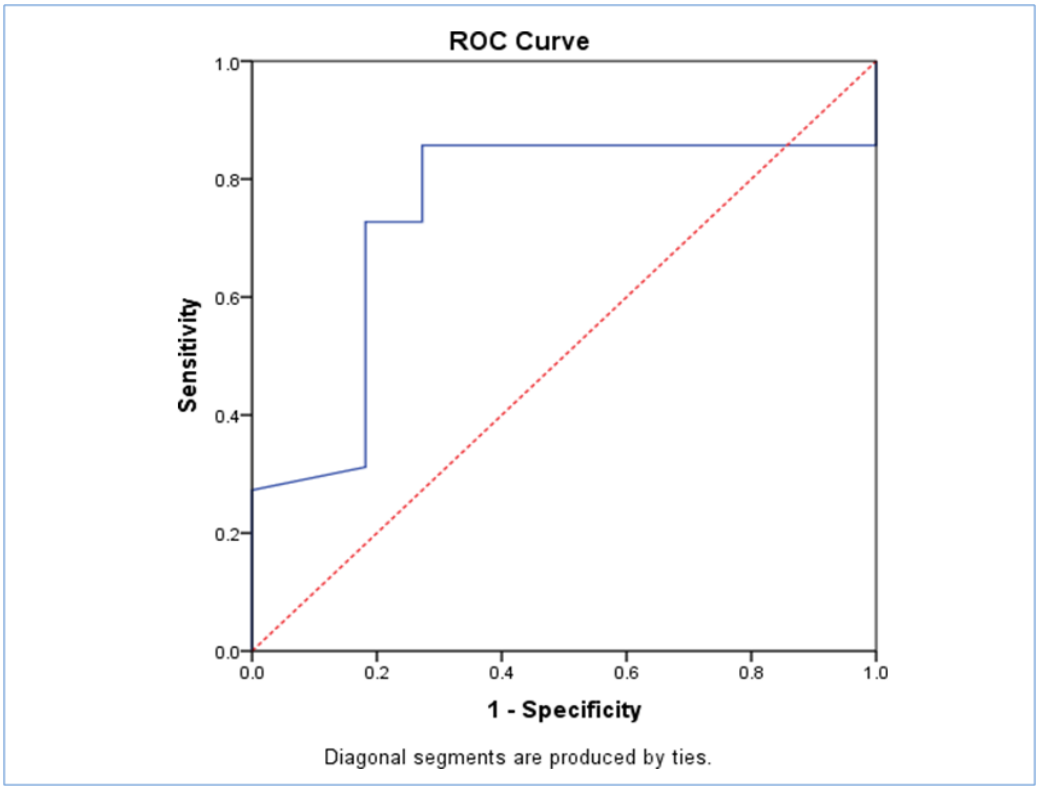

Figure (1): ROC curve of TSB among all cases.

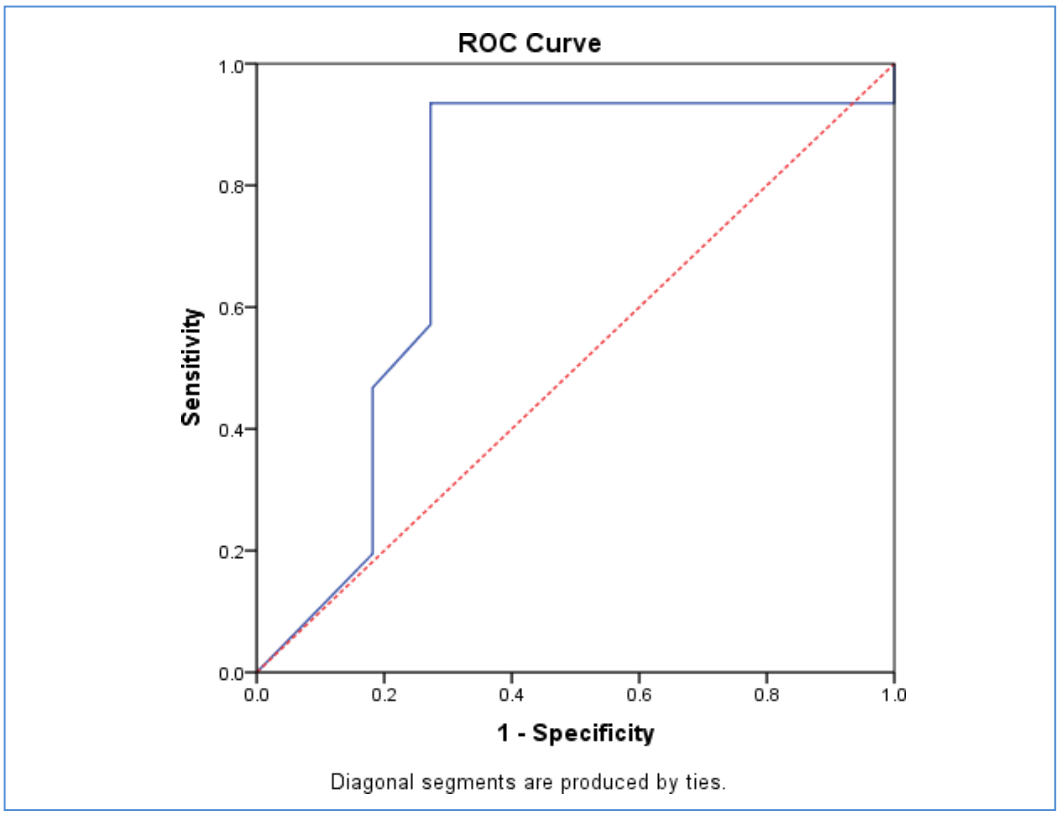

Figure (2): ROC curve of DSB among all cases.

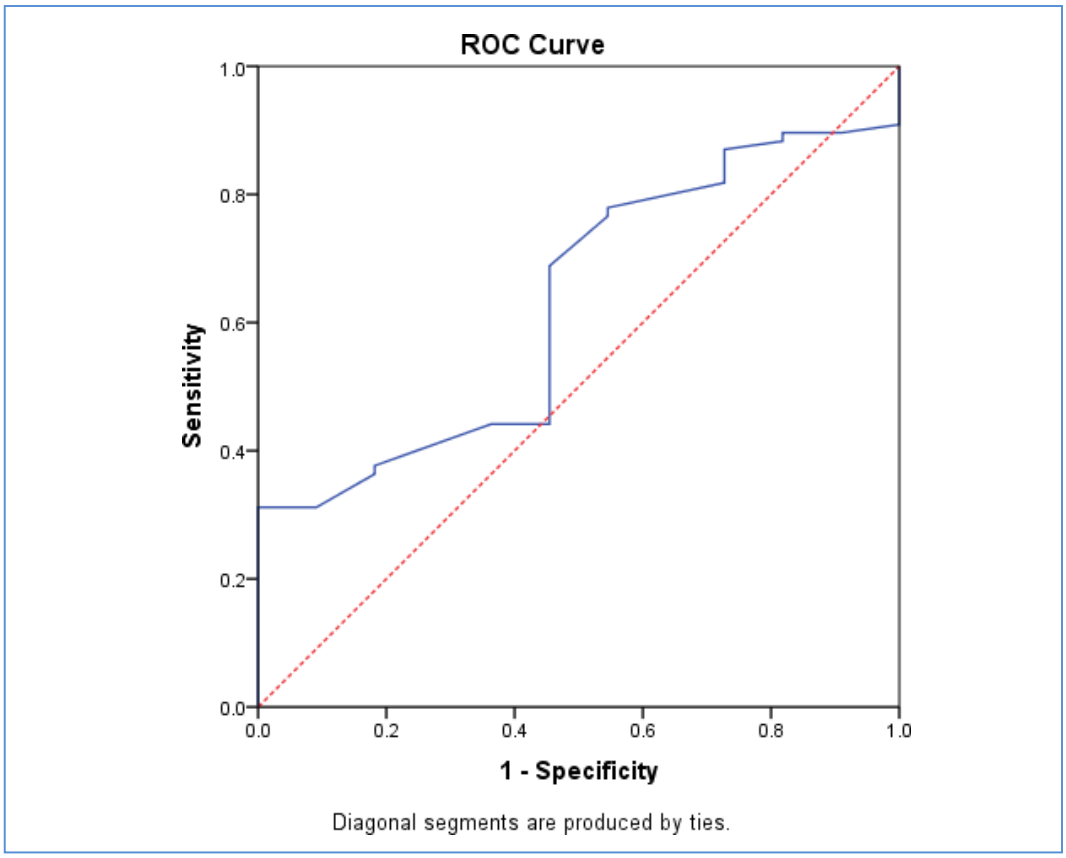

Figure (3): ROC curve of TCB Forehead for detection of jaundice among all cases.

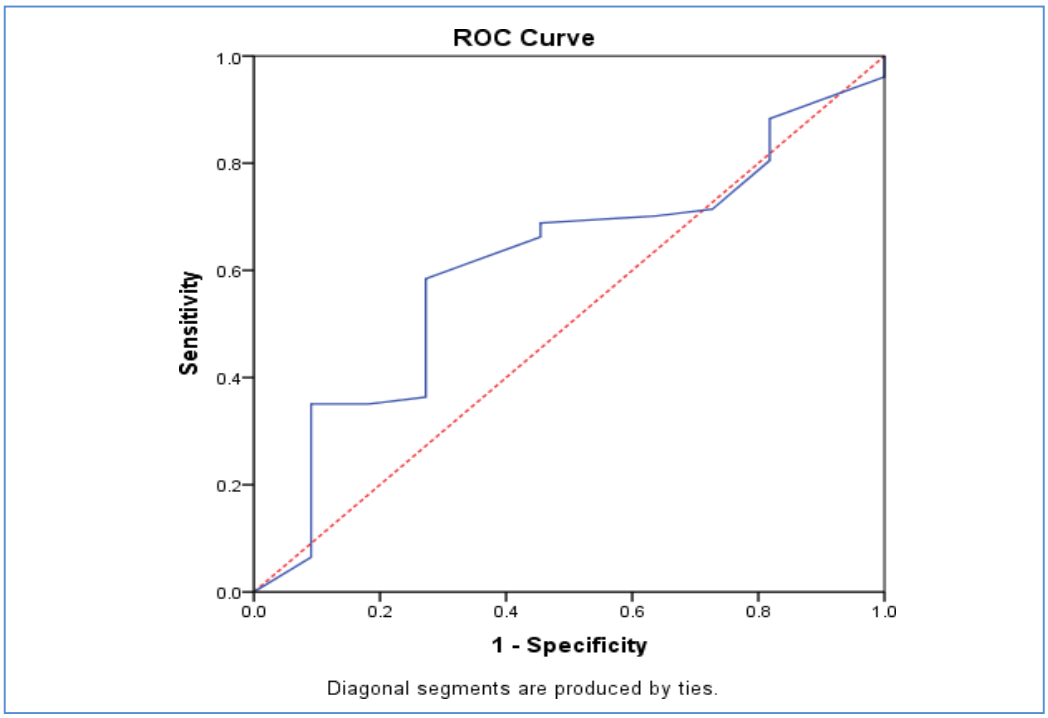

Figure (4): ROC curve of TCB Sternum for detection of jaundice among all cases.

DISCUSSION

Following birth, neonatal hyperbilirubinemia affects more than 50% of term and preterm newborns [7]. Every year, 1.1 million babies are affected by severe hyperbilirubinemia, which is TSB more than 20 mg/dL [8]. It's critical to identify and treat severe hyperbilirubinemia in these newborns as soon as possible to prevent acute bilirubin encephalopathy. Serum bilirubin level measurement is generally considered the gold standard for evaluating newborn hyperbilirubinemia and serving as an indication of phototherapy. TCB measurement instruments provide an alternate method of determining bilirubin levels in environments with limited resources [9].

A total of 88 neonates who had jaundice were included in our study, their gestational ages ranged from 34-39 weeks with a mean of 37.44 ± 0.90. 50 (56.8%) of them were males and 38 (43.2%) were females. Also, 65 (73.9%) neonates their delivery was Cesarean section and 23 (26.1%) their delivery was normal vaginal. 2nd day was the most time of appearance of jaundice (34.1%). The sociodemographic characteristics of the present study patients are similar to that as stated in several researches where male gender was predominant [10-12]. Other previous studies demonstrated that higher bilirubin levels presented in males more than in females [11, 13]. These outcomes suggest an increased susceptibility of male neonates to marked jaundice. In contrast, **Sabzehei *et al.*** [14] reported different results. Also, **Abbas *et al.*** [10] found that, the mean birth weight was 2.62 ± 1.16 kg and most neonates were of gestational age ≥ 37 weeks. This result was consistent with additional research by **Oyapero *et al.*** [11] who found that birth weights of most neonates were between 2.5 and 2.99 kg and they reported that high incidence of neonatal jaundice in term neonates of 37 and 39 weeks. In this concern, a study by **Alcock and Liley** [15] noted that, breastfed newborns often have jaundice between the ages of 24 and 72 hours, which peaks between 5 and 15 days of life and goes away by the third week.

The current study showed that, among 88 neonates, 9 (56.8%) of them were positive consanguinity and previous sibling with hyperbilirubinemia were found in 32 (36.4%) of 3rd sibling. In a previous studies by **Fok *et al.*** [16], **Gale *et al.*** [17], **Corchia *et al.*** [18] and **Scrafford *et al.*** [19] showed that, there is evidence linking an older sibling with neonatal jaundice (NJ) and a lower birth order to a higher risk of NJ. According to **Nielsen *et al.*** [20], there was a 2-3 times higher chance of a recurrence in a woman's subsequent pregnancy if she had given birth to a highly jaundiced child. Additionally, a study by **Kuzniewicz *et al.*** [21] found that, the presence of a family history puts newborns at nearly four times higher risk for severe hyperbilirubinemia raises the possibility that genetic factors may play a role in the genesis of neonatal hyperbilirubinemia. Further research is required because polymorphisms in the genes encoding for uridine diphosphate glucuronosyltransferase 1A1 (the hepatic bilirubin-conjugating enzyme) or other bilirubin metabolism-related enzymes may be significant in determining the likelihood of developing severe hyperbilirubinemia [22, 23].

In this study, Hb was 14.53 ± 2.24 gm/dl and mean TLC was 11.89 ± 2.86 x10^3/mm^3. An earlier study by **Akgul *et al.*** [24] demonstrated that the mean serum hemoglobin level was 15.6 ± 2.3 g/dl. Also, **Abbas *et***

al. [10] noted that the mean initial serum hemoglobin level of their study was 17.54 ± 2.24. In contrast a study by **Thakkar and Shah** [25] reported low hemoglobin level (9.0 gm/dl). In earlier research by **Zhang *et al.*** [26] discovered that there were notable negative correlations between TB and WBCs. First, it has been shown that there are negative connections between TB and inflammatory indicators, which may control the generation of WBCs [27]. Second, a higher WBC count would indicate increased oxidative stress in the cells, which might consume and even deplete natural antioxidants, lowering the quantity of tuberculosis [28]. Third, the correlation between TB and WBC count may have a significant underlying cause, such as metabolic disorders like metabolic syndrome [29].

In the current study, the most blood group of mothers was O (+ve) (60.2%), and the most blood group of babies was B (+ve) (70.5%). Also, most of mothers had positive Rh and 7 (8%) had negative Rh. Our study is in agreement with **Abbas *et al.*** [10] who found that, according to ABO blood groups, high prevalence of neonatal jaundice occurs in patients with blood group O (41.3%). Blood group A was more prevalent (34.7%) than blood group B (22.7%). AB blood group established only 1.3%. Their results were similar with other studies from different regions which reported highest prevalence of jaundice in O blood group neonate and lowest in AB blood group neonate [30, 31].

The present study showed that, the mean of TSB was substantially greater than the mean of TCB at the sternum (P<0.001) and forehead (P = 0.001). In the same line, **Mohamed *et al.*** [32] reported that the mean of TSB was substantially greater than the mean of TCB at the sternum (P = 0.048) and forehead (P = 0.019). Similarly, in a study by **Agrawal *et al.*** [4] the discrepancy between TSB and TCBS measures from the forehead and sternum was analysed by the authors. They found that TSB was overestimated in 66 (29%) forehead and 45 (19.7%) sternum TCB measurements, while TSB was underestimated in 15 (6.6%) frontal and 18 (8%) sternum TCB measurements by more than 2 mg/dL. Significant variations between TSB and TCBs measured across the forehead and sternum have also been documented in previous investigations employing various transcutaneous bilirubinometers [33, 34].

The current study showed that, ROC curve analysis found that cutoff point of TSB in neonates with hyperbilirubinemia was 9.85, with sensitivity of 85.7%, specificity of 27.3% at AUC of 0.743. In this concern, a study by **Spoorthi *et al.*** [35] found that, using a 95% confidence interval and a ROC curve, a cut-off value of 6.15 mg/dl was established with a sensitivity of 82.4%, specificity of 81.8%, positive predictive value of 32.8%, and negative predictive value of 97.6%, along with a highly significant p value of 0.0001. With an area under the curve of 0.91, the test is considered to be satisfactory.

ROC curve analysis found that cutoff point of TCB forehead for detection of jaundice in neonates with hyperbilirubinemia was 7.350, with sensitivity of 89.6%, specificity of 90.9% at AUC of 0.628. Additionally, cutoff point of TCB sternum for detection of jaundice in neonates with hyperbilirubinemia was 3.70, with sensitivity of 88.3%, specificity of 81.8% at AUC of 0.608. **Mohamed *et al.*** [32] reported that, at a TSB level of 205 μmol/L, strong discriminating ability was seen for the TCB forehead (ROC curve = 89.8%) and sternum (ROC curve = 89.7%). There was a range of 84.4% to 85.3% for sensitivity and 77.4% to 76.4% for specificity. With a TSB level of 205 mmol/L, the diagnostic accuracy of the TCB measured at the forehead and sternum showed that there were not variations in terms of sensitivity, specificity, positive and negative predictive values. Conversely, a research by **Agrawal *et al.*** [4] discovered that 79.2% of study participants in the current study were identified as needing phototherapy using forehead transcutaneous bilirubin. Better sensitivity was discovered by the authors at the sternum (87.1%).

CONCLUSIONS

When checking the TCB during phototherapy in a neonate, the forehead was a better site than the sternum. The variations in skin composition that have been noticed in the TCB measurements at the forehead and sternum could be the cause of the observed discrepancies in TCB estimate. This is because the concentration of collagen and melanin can alter the wave length that TCB photometry detects. Measuring TCB rather than TSB may save money, save the need for blood draws, and be a useful screening and monitoring method for jaundiced neonates.

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