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TRANSCUTANEOUS BILIRUBIN LEVELS IN CORRELATION WITH TOTAL SERUM BILIRUBIN IN 50 NEONATES TREATED FOR NEONATAL JAUNDICE AT AL-THAWRA HOSPITAL ALBAIDA –LIBYA

Dr. Najwa H. Abduljawad*[1], Dr. Kamala Omar Yonis[2], Dr. Salem Faraj Hamad[3]

[1]Assistant Professor Department of Paediatrics Al-Thawra Hospital, Albaida – Libya.
[2,3]Department of Paediatrics, Omar Al.Mukhtar University, Al-Baida, Libya.

***Corresponding Author: Dr. Najwa H. Abduljawad**

Assistant Professor Department of Paediatrics Al-Thawra Hospital, Albaida – Libya.

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ABSTRACT

Neonatal hyperbilirubinemia in most of the cases is due to physiological factors, usually is mild and transient. The physiological neonatal hyperbilirubinemia is related to decreased bilirubin clearance from the circulation as a result of relative uridine diphosphate glucuronosyltransferase (UGT) enzyme deficiency and increased enterohepatic circulation. The pathological variety is less frequent and could be caused by immune-mediated hemolysis such as ABO /Rhesus incompatibility, hereditary spherocytosis and elliptocytosis and glucose-6-phosphate dehydrogenase (G6PD) deficiency and pyruvate kinase deficiency. **Aim:** To assess the correlation between transcutaneous bilirubin levels and total serum bilirubin. **Material and methods:** Prospective cohort study of randomly selected 50 jaundiced babies managed at the Neonatal Unit of Al-Thawra Hospital –Albaida City –Libya. The data related to demographic information as gestational age weight, ethnic origin, type of milk feeding, previous use of phototherapy, pre-sternal transcutaneous bilirubin measurement using Bilirubinnometer (DRAEGER JM- 103) and simultaneous total serum bilirubin level (TSB) was collected and analyzed. **Results:** The gestational age ranges between 31-41 weeks with average of 38 weeks. The weight ranges from 1.2-4.3 kg, the average was 2.7 kg. Twenty percent of the cohort were preterm, the postnatal age ranges between 1-15 days with median age of 3.5 days. Only 14% of the group had phototherapy prior to the assessment, 38% had formula milk feeding and 32%. Pre-sternal transcutaneous bilirubin (TCB) ranges between 1.9-17.3 mg/, the total serum bilirubin (TSB) range was 5.16–18.77 mg/dl. **Conclusion:** Data analysis revealed a degree of positive correlation between serum the pre-sternal transcutaneous bilirubin and total serum bilirubin, the correlation coefficient was 0.61.

KEYWORDS: Jaundice, transcutaneous bilirubin, Polycythemia, Bilirubinnometer, Infection.

INTRODUCTION

Hyperbilirubinemia is common and, in most cases, benign problem in neonates. Jaundice observed during the first week after birth in approximately 60% of term infants and 80% of preterm infants. The yellow discoloration usually results from the accumulation of unconjugated non polar lipidsoluble bilirubin pigment in the skin, The unconjugated bilirubin is the end product of heme protein catabolism. During the neonatal period, metabolism of bilirubin is in transition from the fetal stage during which the placenta is the principal route elimination of lipid soluble unconjugated bilirubin, to adult stage, during which the water soluble conjugated form is excreted from hepatic cells into the biliary system and gastrointestinal tract.

MATERIAL AND METHODS

Prospective cohort study of randomly selected 50 jaundiced babies referred or admitted to the Neonatal Unit of Al-Thawra Hospital –Albaida City –Libya. The following data had been collected and analyzed: demographic information gestational age, weight, ethnic origin, type of milk feeding, previous use of phototherapy, pre-sternal transcutaneous bilirubin measurement using Bilirubinnometer (DRAEGER JM-103) and simultaneous total serum bilirubin level (TSB).On-line CORREL function in Excel program was used to analyze the data.

Inclusion criteria is any jaundiced newborn <30 days old, however any neonate with time difference between TCB and TSB with or without phototherapy were excluded from the study.

RESULTS

The gestational age of the cohort ranges between 31-41 weeks with average of 38 weeks, 98 % of patients were of white ethnic origin. The patient weight ranges from 1.2-4.3 kg, the average was 2.7 kg. Ten babies (20%) were preterm, which means they have not completed 37

weeks of pregnancy, the postnatal age ranges between 1-15 days with median age of 3.5 days. Only 7 patients (14%) has phototherapy prior to the assessment, 38% had formula milk feeding 32% had breast feeding and 15% nil per mouth. Pre-sternal transcutaneous bilirubin (TCB) ranges between 1.9-17.3 mg/dl with an average of 10.25 mg/dl. The total serum bilirubin (TSB) range was 5.16–18.77 mg/dl with average of 10.20 mg/dl. Data analysis revealed a degree of positive correlation between the pre-sternal transcutaneous bilirubin and total serum bilirubin, the correlation coefficient was 0.61 (Figures 1&2). There are 43 cases who had no phototherapy prior to the assessment (86% of the total group), in 32 cases (74.4% out of them) there was overestimation of serum bilirubin by transcutaneous bilirubin technique. Fortunately, in about 60% of overestimated results were by <2mg/dl (Table 1). Cases which had phototherapy prior to the assessment were 7cases (14% of total cohort). In all 7 cases the total serum bilirubin readings were underestimated by transcutaneous bilirubin technique (Table 2). Underestimation of serum bilirubin by transcutaneous bilirubin method was seen in 11 cases(25.6% of patients group who had no phototherapy) (Table 3).

Table 1: Overestimation of serum bilirubin by transcutaneous bilirubin technique in cases without phototherapy. 43 cases of the total group (86%) had no phototherapy, in 32 cases out of them (74.4%) there was Overestimation of TCB.

	Overestimation by <2mg/dl N(%)	Overestimation ≥2mg/dl - <3mg/dl N(%)	Overestimation ≥3mg/dl - <5.5mg/dl N(%)
Total number	19(59.3%)	7(21.9%)	6(18.8%)
Male	13(68.4%)	5(71.4%)	1(16.7%)
Female	6(31.6%)	2(10.6%)	5(83.3%)
Weight			
<2.5kg	9(47.4%)	1(14.3%)	2(33.3%)
2.5kg≥	10(52.6%)	6(85.7%)	4(66.7%)
Mean(SD)	2.5(0.688)	3.157(0.77)	2.4(0.53)
Gestational age in weeks:			
<37weeks	8(42.1%)	0(0%)	2(33.3%)
>37weekS	11(57.9%)	7(100%)	4(66.7%)
Mean (SD)	36.9(2.5)	38.79(2.38)	37.4(3.37)
Postnatal age in days:			
<7days	16(84.2%)	6(85.7%)	6(100%)
7days-15days	2(10.5%)	1(14.3%)	0(0%)
>15days	1(5.3%)	0(0%)	0(0%)
Mean(SD)	4.89(4.77)	3.29(1.799)	3.17(1.17)
Colour of skin:			
White	19(100%)	7(100%)	5(83.3%)
Black	0(0%)	0(0%)	1(16.7%)
Feeding mode:			
Formula milk	8(42.1%)	5(71.4%)	3(50%)
Breast milk	7(36.8%)	0(0%)	1(16.7%)
Mixed	0(0%)	1(14.3%)	0(0%)
Nil by mouth	4(21.1%)	1(14.3%)	2(33.3%)
Correlation coefficient	0.981	0.994	0.979

Table 2: Cases which had phototherapy prior to the assessment were 7cases (14% of total cohort). In all 7 cases the total serum bilirubin readings were underestimated by transcutaneous bilirubin technique.

Criteria	N(%)
Total number	7
Male	3(42.9%)
Female	4(57.1%)
Weight	
<2.5kg	1(14.3%)
2.5kg≥	6(85.7%)
Mean(SD)	2.69(0.67)
Gestational age in weeks:	
<37weeks	1(14.3%)
>37weekS	6(85.7%)
Mean (SD)	37.9957(2.8)
Postnatal age in days:	
<7days	5(71.4%)

7days-15days	2(28.6%)
>15days	0(0%)
Mean(SD)	5.57(2.88)
Colour of skin:	
White	7(100%)
Black	0(0%)
Feeding mode:	
Formula milk	1(14.3%)
Breast milk	5(71.4%)
Mixed	0(0%)
Nil by mouth	1(14.3%)
Correlation coefficient	0.8

Table 3: Underestimation of serum bilirubin by transcutaneous bilirubin method was seen in 11 cases (25.6% of patients group who had no phototherapy).

Criteria	Underestimation by <2mg/dl	Underestimation by >2mg/dl and <3mg/dl
Total number	9(81.9%)	2(18.1%)
Male	5(55.6%)	2(100%)
Female	4(44.4%)	0(0%)
Weight		
<2.5kg	2(22.2%)	1(2.3%)
2.5kg≥	7(77.8%)	1(2.3%)
Mean(SD)	3(0.6)	2.85(0.9)
Gestational age in weeks:		
<37weeks	3(33.3%)	1(2.3%)
>37weekS	6(66.7%)	1(2.3%)
Mean (SD)	37.43(2)	38.995(3)
Postnatal age in days :		
<7days	5(55.6%)	2(100%)
7days-15days	2(22.2%)	0(0%)
>15days	2(22.2%)	0(0%)
Mean(SD)	8.67(8.559)	5(1.4)
Colour of skin:		
White	9(100%)	2(100%)
Black	0(0%)	0(0%)
Feeding mode:		
Formula milk	3(33.3%)	1(50%)
Breast milk	4(44.4%)	0(0%)
Mixed	0(0%)	1(50%)
Nil by mouth	2(22.2%)	0(0%)
Correlation coefficient	0.972	1

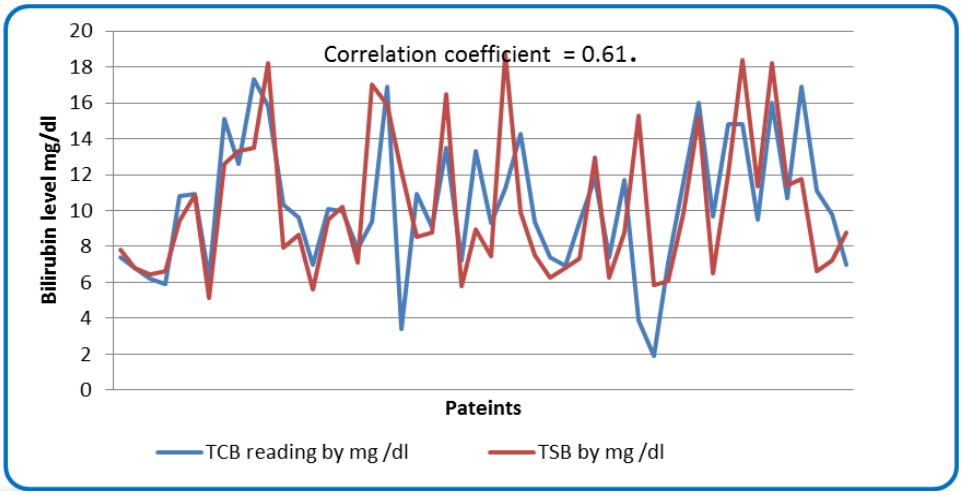

Fig. 1: Correlation between pre-sternal transcutaneous bilirubin and total serum bilirubin levels in 50 neonates with jaundice.

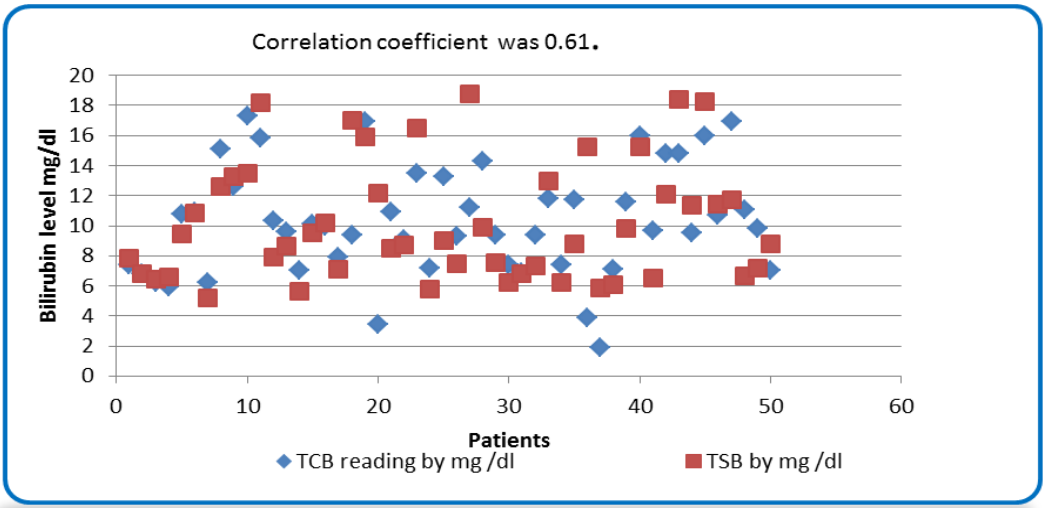

Fig. 2: Correlation between pre-sternal transcutaneous bilirubin and total serum bilirubin levels in 50 neonates with jaundice.

DISCUSSION

Unconjugated hyperbilirubinemia may be caused or increased by any factor that:

1. Increases the load of bilirubin to be metabolized by the liver e.g hemolysis (glucose-6-phosphate dehydrogenase (G6PD) deficiency (Fig.3), Pyruvate kinase (PK) deficiency) polycythemia, shortened red blood cells life as a result of immaturity or transfusion of cells, increased enterohepatic circulation, infection.[1]
2. Damages or reduces the activity of the transferase enzymes or other related enzymes as the enzymes responsible for bilirubin conjugation as glucuronosyl transferase (genetic defect, hypoxia, infection, thyroid deficiency).[1]
3. Leads to a reduction of bilirubin uptake by the liver due to deficiency/decreased levels of some essential factors as ligandin (a bilirubin binding protein (genetic defect and prematurity).[2]

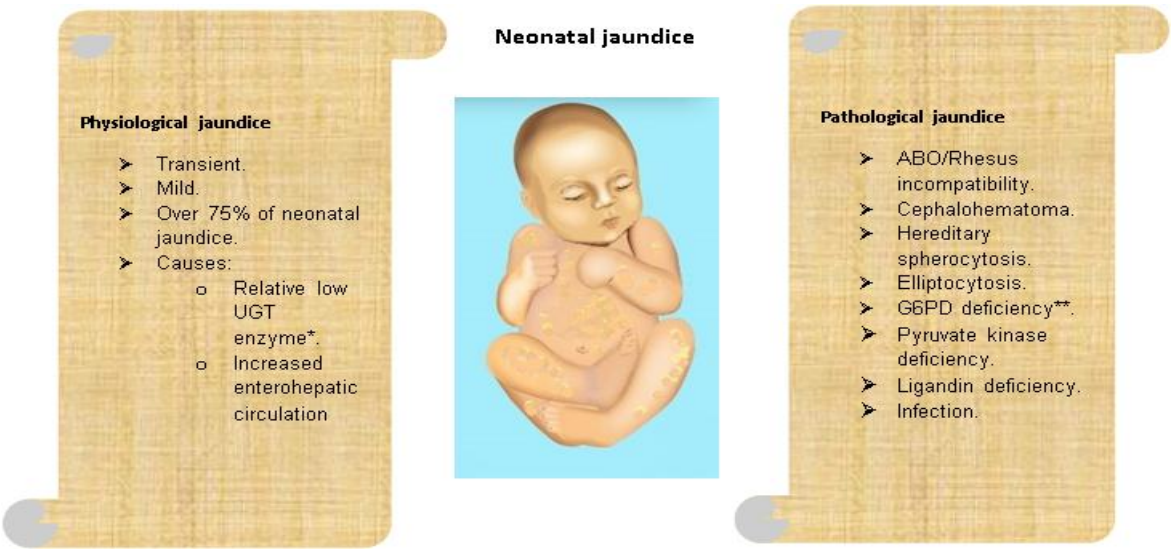

Figure 3: Causes of neonatal jaundice.

*UGT: Uridine diphosphate glucuronosyl transferase.
** Glucose-6-phosphate dehydrogenase.

According to the UK Cancer Research data, liver malignancy is more common in adults where it occupies the 03rd place in the cancer-related mortality list after lung and colon,[3] in infants and children is rare and seldom presented with jaundice.[4]

Jaundice usually appears during the early neonatal period, depending on etiology. jaundice usually becomes apparent in cephalocaudal progression, starting on the face and progressingto the abdomen and then the feet, as serum level increase. (face ~5mg/dl; mid abdomen~15mg/dl; soles ~20mg/dl). But clinical examination can not be depend on to estimate serum levels, but blood analysis still the most accurate to measure the bilirubin level. The greatest risk associated with indirect hyperbilirubinemia is the development of

bilirubin neurologic dysfunction (kernicterus).There are reported major risk factors associated with the development of severe hyperbilirubinemia in near term or term infants e.g High-risk range of pre-discharge TSB or TCB, jaundice observed in the first 24 hours after birth, preterm birth, G6PD deficiency and blood group incompatibility with positive direct anti-globulin test.[5]

Transcutaneous bilirubin measurement is simple, cost saving and non invasive tool, where many previous studies have recommended to be as used as a screening tool in the neonatal units as the technique has a high predictive value.[6] Also the use of TCB will allow reduction in blood bilirubin samples for TSB after the implementation of TCB as will as potential better resources utilization.[7] Chimhini et al in 2018, published study where two hundred and eighty-three Zimbabwean newborns were recruited between 01st August and 30th November 2012. The authors analyzed the correlation between serum and pre-sternal transcutaneous bilirubin and between serum and forehead transcutaneous bilirubin. They found that there is no difference between forehead and sternal site for cutaneous bilirubin accuracy in comparison with serum bilirubin,[8] the correlation between serum and TCB (sternum) was 0.77 and between serum and TCB (forehead) was 0.70. the device used in Chimhini study was (DRAEGER JM 103), the same device that used in our study.

Yang et al in 2019, reported that, there is a positive correlation between TCB and TSB before during and after phototherapy in term and late term infant.[9] This is in contrary with the Nagar and Kumar from 2017study who had reported that that TCB level measured by JM-103 device is unreliable for estimating real bilirubin levels during phototherapy among preterm newborns. However, TCB-TSB agreement improved substantially after completion of phototherapy, this may encourage the clinicians to use a such TCB device in similar scenarios could lead to a reduction in blood sampling during the post-phototherapy phase.[10] Andra kurnianto et al in 2017, reported that TCB cutoff point of >5mg/dl had sensitivity of 100%, specificity was 83%, 99.3% positive predictive value, 100% negative predictive value.[11] A large retrospective study published by Olusanya et al in 2017, they have analyzed a data of 12,377 TCB levels performed for 6,373 neonates in the first postnatal week, the study covered r a period of 48 months using Bilichek and JM-103 bilirubinometers. The study concluded that, the predictive utility of TCB as a probable screening tool varies across devices in black African neonates with or without risk of significant hyperbilirubinemia, and showed readings lower than levels reported in non-black neonates.[12] Surana et al in 2017, enrolled 160 neonates in their study. The aim was to to assess the correlation between TCB and TSB levels in neonates. Their results revealed that TCB and TSB correlation sensitivity was 100% with TSB >10 mg/dl, and decreased to 92% with TSB >15mg/dl, the specificity was 23% with TSB >15mg/dl and 79% with TSB >10mg/dl. They have concluded that, TCB correlated well with TSB levels and showed good sensitivity and satisfactory specificity, thus validating its use as a screening tool for evaluation of jaundice in newborns.[13] The above data prompted us to conduct this research is to reduce frequent unnecessary blood samplingas much as possible (after confirmation of good correlation), in addition to that this tool is recently introduced to our hospital and was not previously validated through a similar study at Al-Thawra Hospital.

CONCLUSION

The study demonstrated a degree of positive correlation of pre- sternal transcutaneous bilirubin measurement and total serum bilirubin in this cohort of Libyan children, this means that TCB is recommended technique for monitoring bilirubin levels.

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