VALIDITY OF VISUAL ASSESSMENT OF NEONATAL JAUNDICE FOR SCREENING SIGNIFICANT HYPERBILIRUBINAEMIA

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ABSTRACT

Objective: To determine the validity of absence of visual jaundice below nipple line in ruling out significant neonatal hyperbilirubinaemia.

Study Design: Cross-sectional study.

Place and Duration of Study: PNS Shifa Hospital Karachi Pakistan, from Jan to Aug 2017.

Patients and Methods: A total of 284 babies with ages ranging between 2-7 days, more than 35 weeks of gestation and more that 2000 grams of weight, were enrolled. Visual assessment of dermal jaundice was done in these neonates by a trained pediatric resident. Two zones were arbitrarily defined; one above nipple line and the other below it. The point of most distal dermalicterus was recorded on proforma mentioning the corresponding zone. Serum samples were then sent for laboratory measurement of total bilirubin within one hour of visual assessment. Jaundice in these zones was compared with corresponding total serum bilirubin. Significant hyperbilirubinaemia was defined as total serum bilirubin (TSB) more than 205 micromol/litre.

Results: Parents of 4 babies (1.61%) did not give consent for the blood test and 31 babies (10.91%) were lost to follow up. Data of remaining 249 neonates revealed that absence of visual jaundice below the nipple line had sensitivity of 100% and specificity of 73.23% in ruling out significant hyperbilirubinaemia.

Conclusion: Absence of jaundice below the nipple line was a reliable screening tool for screening significant hyperbilirubinaemia after 24 hours of age in otherwise healthy babies more than 35 weeks of gestation and more than 2000 grams of weight.

Keywords: Hyperbilirubinaemia, Jaundice, Newborn, Phototherapy.

INTRODUCTION

Jaundice is one of the most common causes of medical attention in neonates[1]. Approximately 50-70% of the term babies and 80% of the preterm babies develop jaundice within seven days of life[2]. Close observation of bilirubin level and its trend in affected newborns is required, as very high serum bilirubin levels may cause neurological damage and even death[3]. Jaundice within 24 hours signifies a high rate of bilirubin production and requires immediate care and management[4]. After this age significant hyper-bilirubinaemia is the total serum bilirubin (TSB) above the threshold level that may require medical intervention like phototherapy and/ exchange transfusion. Its value varies accor-ding to gestational and postnatal ages but is 205 µmol/L in neonates >35weeks of gestation at 24 hours of age[5].

Total serum bilirubin (TSB) measurement is the gold standard test[1] to identify those with significant hyperbilirubinaemia (around 10%) from those who don't require intervention (around 90%)[4]. As serial TSB is costly and punctures for the test are painful,some parents loose compliance and skip surveillance of their neonates' bilirubin level[6]. Transcutaneous bilirubinometry (TCB) is the most widely accepted alternative, as it is reliable and painless[7]. When available, TCB is used to screen the jaundiced neonates[7]. TSB becomes indicated when TCB reaches at or crossesthe threshold of significant hyperbilirubinaemia[5]. Due to high cost of the TCB equipment, it may not be available in

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resource limited settings whereone has to resort to TSB for screening and subsequent monitoring[5].

Cephalocaudal progression of neonatal jaundice (Kramer's rule) is well known[1]. In resource limited settings, in the absence of costly TCB equipment, clinicians usually resort to visual assessment to screen neonatal jaundice for significant hyperbilirubinaemia[6]. Although the accuracy and reliability of visual assessment is uncertain[5], some evidence suggests that absence of jaundice below the nipple line correlates with TSB levels <205µmol/L[8]. If valid, this may obviate the need of many unnecessary skin punctures in resource limited settings where TCB is not available.

Neonatal jaundice is common in our population[9] and there is paucity of local studies on validity of its visual assessment[10]. Therefore our study aims to examine the help of visual assessment of neonatal jaundice as a screening tool.

PATIENTS AND METHODS

This cross-sectional study was conducted in neonates from postnatal ward and outpatient department in PNS Shifa Hospital over 8 months from 1st January to 31st August 2017. A convenience sample of visibly jaundiced neonates more than 35 weeks of gestation, 24 hours of postnatal age and >2000 grams of weight were included. Exclusion criteria was neonates who had jaundice extending to palms and soles (as this much jaundice almost always means TSB >205micromol/litre), who received phototherapy within last 24 hours, had blood group in compatibility, conjugated hyperbilirubinemia, anomalies of the trunk or lower limbs, sepsis or were otherwise unwell with other complaints. As sample size of similar studies ranged from 50-500 approximately therefore 284 neonates were enrolled. Out of these, 31 babies were not brought to follow up with laboratory report after visual assessment. Parents of 4 babies (1.61%) did not give consent for the blood test. Therefore, data of 249 neonates was completed. Clinical assessments of jaundice were recorded by a physician who had a minimum of 6 months of postgraduate residency work experience in pediatrics in a tertiary hospital. Parents of the patients were explained about the study and their consent was obtained. Approval from ethical committee of PNS Shifa Hospital was also obtained. Infants were observed unclothed in warm environment, under indoor lighting augmented by natural daylight from clinic windows. The most distal point of jaundice was found with application of skin pressure. The body was arbitrarily divided into two zones, upper zone (UZ) and lower zone (LZ) as shown in the figure. Upper zone (UZ) was considered negative for significant hyperbilirubinaemia and lower zone (LZ) was considered positive. TCB facility was not available in the hospital therefore blood for plasma bilirubin was obtained and sent to the laboratory of PNS Shifa hospital within one hour. Samples were processed in Roche Cobas 6000 Fully Automated Chemistry Analyzer with Roche reagents, calibrator and controls by Diazo method. TSB less than 205micromol/litre was taken as negative and more than 205

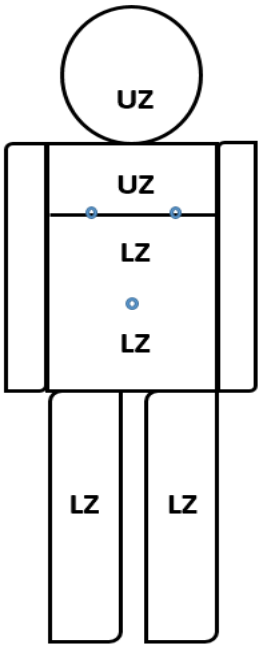

Figure: Division of body in two zones by nipple line for visual assessment of jaundice. UZ = Upper zone, LZ = Lower zone.

micromol/litre as positive for significant hyperbilirubinaemia. Descriptive statistics were calculated for quantitative and qualitative variables. A 2×2 table diagnostic test was employed in this study to analyze the data. Sensitivity, specificity, positive and negative predictive values were calculated with Microsoft Excel 2007.

RESULTS

Among these 249 neonates, 148 (59.44%) were males and 101(40.56%) were females. Mean age was 98.5 hours (range from 25-166 hours). Results showing number of neonates falling in the two zones and their corresponding TSBs are summarized in table. Calculation from 2x2 table revealed that absence of visual jaundice below the nipple line had sensitivity of 100% and specificity of 73.23% of ruling out significant hyperbilirubinaemia. It had positive predictive value of 78.2% and negative predictive value of 100%. This means that visual presence of jaundice below the nipple line may not be accurate in predicting significant hyperbilirubinaemia but its absence reliably rules out significant hyperbilirubinaemia.

Table: Visual Assessment for significant hyperbilirubinaemia.

		Number of Jaundiced neonates	
		Upper zone (U)	Lower zone (L)
Total serum bilirubin	Less than 205 micromol/litre	93	34
	More than 205 micromol/litre	0	122

DISCUSSION

Apart from visual assessment and TCB, many studies have investigated other low cost, minimally invasive or non-invasive methods for bilirubin estimation. Examples of minimally invasive methods are Bilistick[11] or BiliSpec[12] (point-of-care system) and of non-invasive methods are Icterometer[13] (It compares jaundice with a chart having grades of yellow colour), BiliCam[14]/Biliscan[15] (Both consist of smartphone-based device that uses the on-device camera to monitor jaundice in newborns) and scleral image interpretation[16]. All these studies aim to prevent unnecessary TSB estimations.

Presently the utility of visual assessment of neonatal jaundice has been validated in only two main scenarios. Firstly if jaundice is not visible there is no need for TCB or TSB[5]. Secondly jaundice extending to the distal extremities correlates well with significant hyperbilirubinaemia and it should be evaluated by TSB[6]. Our study provides a reliable, safe, non-invasive clinical tool with no cost for screening neonatal jaundice especially in resource limited settings. Similar studies have been done in Jordan[8] and USA[17].

The study in Jordan found that visual assessment of neonatal jaundices considering the nipple line as the landmark for threshold had sensitivity of 100% and specificity of 56.07%[8]. The sensitivity is same as was found in our study. The difference in specificity may be due to difference in skin color or training of physicians or quality of standardization of the visual inspection.

The study conducted in an urban public hospital in the USA showed that absence of jaundice in the lower chest had negative predictive value of 94% in ruling out serum bilirubin levels above 205 micromol/litre[17]. This is in accordance with our finding.

Another study was evaluated maternal appreciation of this threshold. It was found that jaundice extending below the nipple line had a positive predictive value of 55% and a negative predictive value of 86% for identifying infants with bilirubin levels of more than 205 micromol/litre[18]. The difference in the values from our findings may be related to more professional experience of observers in our study.

A big concern with visual assessment is its subjective nature. Studies have shown difference in accuracy among people with different levels of the skill[17]. However evidence showed that best agreement among pair of observers was seen at

the 'nipple line to umbilicus' site[17]. In these studies there is a tendency to over-estimate rather than underestimate bilirubin. If the observer over estimates jaundice thus assigning incorrectly the lower zone while the jaundice was not below the nipple line, it will only trigger TSB estimation and correct bilirubin value will be obtained. Over-estimation occurred in 34 babies in our study. The real concern is under-estimation (incorrect assignment of upper zone while the bilirubin was more than 205micromol/litre) thus falsely labelling the neonate in safe zone. Not a single such instance was found in our study. The reason may be that many studies suggest correlation of neonatal jaundice around nipple/ mid-chest level with TSB value between 100-150 micromol/litre. This still leaves 55-105 micromol/litre as margin for error when subtracted from the value of 205 micromol/litre for those who under-estimate. If subcostal level would have been used instead of nipple line this margin of error might have been become smaller thus increasing the specificity but decreasing the sensitivity. In our study 93 babies were correctly identified to be in the safe zone and TSB could be avoided in these perfectly healthy babies.

Simplicity of this tool makes it feasible for its general use. Studies have shown benefit of teaching visual assessment to even parents as they were shown to be able torecognize significant jaundice[18].

Serial observations at smaller intervals are recommended especially when rapid progression of jaundice is expected as in blood group incompatibility, cephalhaematoma or subapeneurotic haemorrhage[4].

Skin color due to ethnic differences may affect judgment in visual assessment especially in dark coloured babies[5] therefore the result of small studies could not be generalized.

We excluded preterm neonates <35 weeks of gestation and <2000 grams in our study.In these neonates jaundice is more easily visible because of immature skin and they have differences in bilirubin-albumin binding. Therefore progression of dermal icterus may have differences as compared to term or near term neonates[19].

This study has another limitation as we have taken a single value as threshold of significant hyperbilirubinaemia (TSB >205 umole/L).It is valid at 24 hours of age and increases with age till 96 hours from birth and then becomes static. It also varies for the gestational age at birth. We chose this value as this is safer especially considering that day 2 is the commonest age of discharge of the newborns from hospital[20]. In some studies value of 250micromol/litre was selected as cut-off[6]. Choice of our value has increased the sensitivity but has the opposite effect on specificity. This makes visual assessment a good screening tool to trigger TSB estimation. Other studies may be required to validate distal anatomical landmarks as visual screening threshold e.g. subcostal or umbilical levels, may be in neonates >96 hours of age.

Use of scleral color digital photography can identify subjects with TSB above 205 µmol/l with sensitivity of 100% and specificity of 50%[16]. The absence of visual conjunctival icterus has been found to be helpful to rule out significant hyperbilirubinaemia[21]. Its combination with visual assessment of dermal icterus may improve the accuracy of screening process. These clinical tools may be combined with other minimally or non-invasive tool to improve sensitivity and specificity as compared to serum blood sampling results.

CONCLUSION

In neonates more than 35 weeks of gestation and >2000gms of weight, absence of jaundice below the nipple line was found reliable screening tool for ruling out significant hyperbilirubinaemia, after 24 hours of life in otherwise healthy neonates. When TCB is not available this tool may obviate the need of many unnecessary skin punctures.

CONFICT OF INTEREST

This study has no conflict of interest to be declared by any author.

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