Original Article

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Association of Dermal Icterus with Serum Bilirubin in Newborns Weighing <2000 Grams

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ABSTRACT

Background: Neonatal hyperbilirubinemia is a common neonatal problem, with the rise of serum bilirubin there is a corresponding cephalocaudal progression. We are conducting this study to evaluate the strength of association with cephalocaudal progression.

Objective: To determine whether the clinical observation is predictable in evaluating the extent of jaundice and then to evaluate the reliability of visual assessment as an indication for the measurement of serum bilirubin level. Whether visual assessment is helpful in the management of jaundiced babies when and where serum bilirubin estimation facilities are not available.

Materials and Methods: The study was conducted to find the relation of dermal icterus with serum bilirubin in babies weighing <2000 g. The point of most distal progression of dermal icterus is determined by blanching the skin with the pressure of the thumb and noting the color of underlying skin when the thumb is removed in a well-lighted room.

Results: The study was conducted on 100 newborns delivered in the Department of Obstetrics and Gynecology, admitted to Neonatology section of Department of Paediatrics, Government Medical College Patiala. 15 babies had double observation, so a total number of observation was 115. The jaundice was clinically assessed in various dermal zones in natural daylight and total and differential bilirubin was estimated. The statistical analysis comparing serum bilirubin with dermal zones is significant in all dermal zones ($P < 0.05$) except between zones IV and V ($P > 0.05$). The statistical analysis was not significant ($P > 0.05$) comparing male and female newborns.

Conclusion: A reliable association is noted between serum bilirubin and cephalocaudal progression of dermal icterus. The association holds true for lower bilirubin (dermal Zones I-III) level, but with the progression of dermal icterus beyond dermal Zone III, serum bilirubin estimation is mandatory.

Key words: Encephalopathy, Hyperbilirubinemia, Icterus, Infants

INTRODUCTION

Neonatal jaundice is the yellow discoloration of the skin and sclera of neonates caused by hyperbilirubinaemia. Bilirubin is a yellow pigment that is produced in the body during the normal recycling of aged red blood cells. About 50% of term and 80% of preterm infants develop jaundice in the 1st week of life.[1]

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Several risk factors have been identified such as an increased bilirubin load in the hepatocytes as a result of reduced erythrocyte survival, rapid enterohepatic circulation and increased erythrocyte volume. Hyperbilirubinemia is more exaggerated in low birth weight because of the reduced life span of erythrocytes, gastrointestinal immaturity, delayed postnatal maturation of hepatic bilirubin uptake and conjugation. In addition, there is a delay in enteral feeding in sick low birth weight which may lead delay in colonization of intestinal tract of leading to enhancement of bilirubin enteohepatic circulation. These contribute to greater degree and duration of neonatal jaundice in low birth weight babies. Low birth weight and preterm birth are major risk factors for exaggerated hyperbilirubinaemia.[2] clinically significant levels that warrant treatment occur in approximately 50-80% of preterm neonates. Preterm

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infants are at risk of bilirubin encephalopathy at lower total serum bilirubin levels than mature infants.[3]

The increase in total serum bilirubin is accompanied by the progression of dermal icterus from, face to trunks and extremities finally to palms and soles. Hyperbilirubinemia can be safely rule out by eye if jaundice does not reach abdomen or the extremities dermal Zones I and II.[4] The color usually results from accumulation of skin and mucous membranes of unconjugated, nonpolar, lipid soluble bilirubin pigment. Neonatal dermal icterus is not noticeable at serum bilirubin <4 mg/dl.[4]

Pediatrician believes that icterus is a reliable clinical finding among examiners, and its progression and intensity in neonates reflect the degree of rise of serum bilirubin concentration. The cephalocaudal progression was first noted by Kramer in 1969 and found a correlation between the cephalocaudal progression and serum bilirubin with a wide range of bilirubin concentration for jaundice in each dermal zone.[5]

In the present study, we have evaluated the reliability of visual assessment in describing the intensity of jaundice in newborns weighing <2000 g.

MATERIALS AND METHODS

The study was conducted to correlate dermal icterus with serum bilirubin in newborns weighing <2000 g. The study protocol was approved by the Local Ethical Committee, and parental informed consent was obtained. The study period was from August 2004 to July 2006. The newborns were delivered in the Department of Obstetrics and Gynecology and admitted in a neonatal section of Department of Pediatrics, Government Medical College/Rajindra Hospital, Patiala, Punjab, India. Total and differential serum bilirubin was estimated in Department of Biochemistry. The newborns were randomly selected. The weight of babies was taken at birth. All babies weighing more than 2000 g were excluded from the study. The gestation of newborns ranged from 26 to 41 weeks. The cases were divided arbitrarily into two groups 26-36 weeks (pre-term) and 37-41 weeks as term. Statistical analysis of the cephalocaudal progression of dermal icterus associated with an increase in serum bilirubin was done by using unpaired *t*-test.

Examination of babies was conducted in well-lighted room under natural light. The correct evaluation of dermal icterus is dependent on the amount of lightening. Yellow-white artificial lightening, yellow walls can be extremely misleading. All babies were examined once every 24 h till baby is placed under phototherapy. The dermal icterus is noted in different dermal zones as shown in Figure 1, dermal Zone I (head and neck), dermal icterus 2 (trunk to umbilicus), dermal Zone III (Groins including upper thighs), dermal Zone IV (knees and elbows to ankles and wrist), dermal Zone V (feet and hands including palms and soles) as shown in Figure 1. The point of most distal progression of dermal icterus is determined by blanching the skin with the pressure of the thumb and noting the color of underlying skin when the thumb is removed. All observations in this study were done by one person, and all bilirubin is processed by one person. Total and serum bilirubin was estimated by Malloy and Evelyn method.[6]

RESULTS

The study was conducted on 100 Newborns. The jaundice was clinically assessed in various dermal zones in natural daylight from 1st day of life. 15 babies had double observations, so a total number of observations was 115. Figure 2 showing serum bilirubin in different dermal zones, out of 115 observations, 4 were made in dermal Zone I; range indirect serum bilirubin was 3.7-5.4 mg/dl with mean of 4.32 ± 0.74. 32 observations were made in dermal Zone II, with a range of 4.1-11 mg/dl with a mean of 7.82 ± 1.59. 48 observations were made in dermal Zone III with a range of 6.8-13.5 mg/dl with a mean of 10.64 ± 1.18. 25 observations were made in dermal Zone IV with a range of 9.2-14 mg/dl with a mean of 11.47 ± 1.37. 6 observations were made in dermal Zone V with a range of 11.4-20 mg/dl with a mean of 13.77 ± 3.17.

Table 1 showing statistical analysis of rise of serum bilirubin in different dermal zones which is significant ($P < 0.001$) in all dermal zones except for dermal Zones IV and V where it was not significant ($P > 0.05$). Figure 3 showing comparison between males and females for the rise of serum bilirubin in different dermal zones, after that statistical analysis is shown in Table 2 found no difference in progression of jaundice with serum bilirubin based on gender ($P > 0.05$).

Table 1: Statistical analysis which was significant in all dermal zones (*P*<0.05) except in zones IV and V where it was insignificant (*P*>0.05)

Dermal zones	Unpaired *t*-test	*P* value	Significance
II and III	8.54	<0.001	HS
II and IV	9.35	<0.001	HS
II and V	4.50	<0.001	HS
III and IV	2.57	<0.05	S
III and V	2.40	<0.05	S
IV and V	1.75	>0.05	NS

S: Significance, HS: High significance

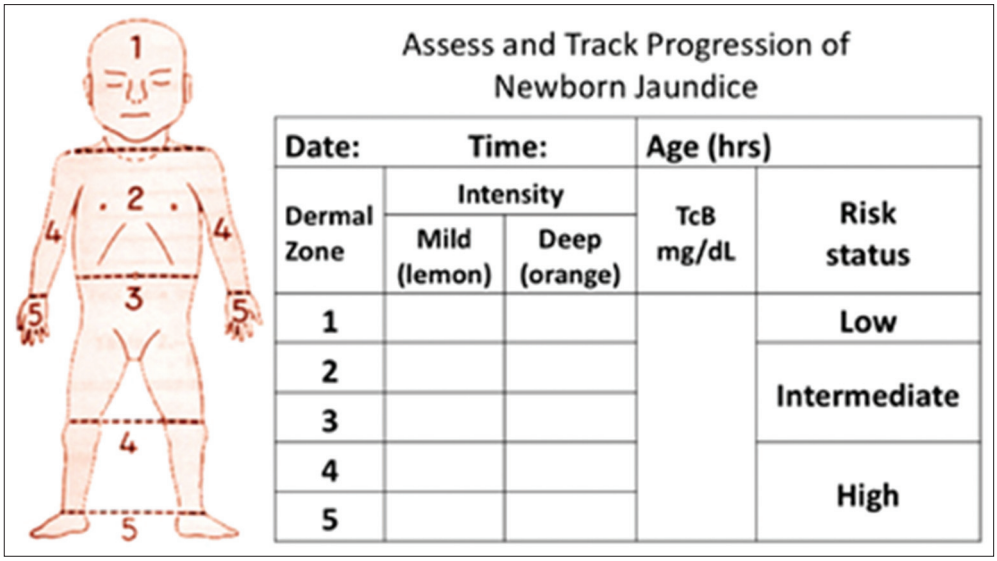

Figure 1: Different dermal zones for assessment of progress of jaundice

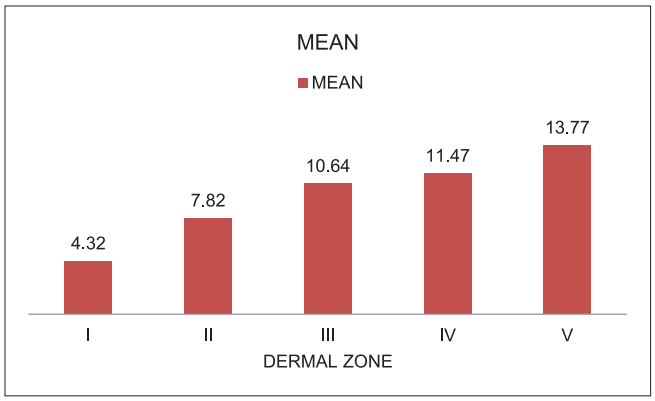

Figure 2: Serum bilirubin in Newborns in different dermal zones

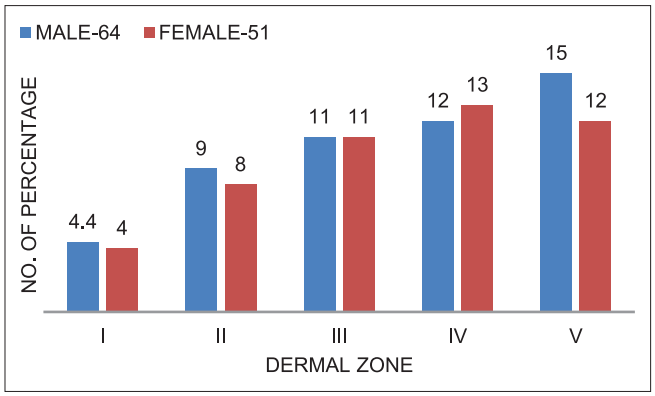

Figure 3: Comparing dermal icterus with serum bilirubin comparing gender

Table 2: Statistical analysis comparing of serum bilirubin in different dermal zone comparing gender

Dermal zones	*t*-test	*P* value	Significance
II and III	0.31	>0.05	NS
III and IV	0.21	>0.05	NS
IV and V	1.2	>0.05	NS

S: Significance, HS: High significance

DISCUSSION

The present study confirms the presence of cephalocaudal progression associated with a rise in serum bilirubin. The American Academy of Pediatrics recommendations for management of hyperbilirubinemia presumes that clinical examination will be sufficient for identification of infants who needs serum bilirubin testing.[7]

In present study serum bilirubin in newborns in different dermal zones is shown in Figure 1, statistical analysis was significant ($P < 0.05$) in dermal Zones I-III but progression beyond dermal Zone III, correlation was not significant ($P > 0.05$). The mean values of indirect serum bilirubin in the present study were different from that reported by Kramer (1969). Kramer made 198 observations of 108 fullterm infants, 82 observations on 40 newborns weighing <2000 g were taken. The comparison of values in present study with that of Kramer has been shown in Table 3.[5]

The present study was in low birth weight babies in which icterus is more easily visible because of immature skin and different bilirubin-albumin binding hence progression of dermal icterus is more rapid as compare to term infants.[8]

Various studies evaluated factors associated with the accumulation of bilirubin in the skin like lipid content of skin, the difference in permeability of albumin in capillaries, local skin perfusion. The cephalocaudal progression is due to conformational changes in newly formed bilirubin albumin complex.[9-11] This conformational change is achieved in 8 s after formation. The reticuloendothelial system (liver and spleen) is site for production of bilirubin hence initial staining

Table 3: Comparison of rise of bilirubin with cephalocaudal progression of dermal icterus from Kramer with present study

	Kramer			Present study		
Dermal zone	Number of observation	Range of serum bilirubin	Mean	Number of observation	Range of serum bilirubin	Mean
I	2	4.1-7.5	-	4	3.7-4.2	3.9±0.2
II	14	5.6-12.1	9.49±1.9	28	5.2-11	7.93±1.7
III	8	7.1-14.8	11.4±2.3	37	6.8-12.2	10.76±1.12
IV	24	9.3-18.4	13.3±2.1	21	8-14	11.48±1.46
V	34	>10.5	-	9	11.4-20	13.6±2.9

in central part of body including head and then with increase in bilirubin concentration.[12-14] Bilirubin may be transferred to the skin through two different mechanisms: (1) by leakage of bilirubin-albumin from plasma into extravascular spaces and (2) by precipitation of bilirubin acid in phospholipid membranes. A considerable amount of serum albumin is found outside the blood stream; the extra vascular albumin constitutes about 60% of total in adults. Since bilirubin is bound with albumin and bilirubin-albumin distribution will depend on the distribution of albumin, skin contains a significant amount of albumin hence in cases of hyperbilirubinemia the skin will assume yellow color due to albumin-bilirubin content. Another mechanism is the formation of bilirubin acids when plasma of icteric neonates is saturated with bilirubin acids, the compound to will be precipitated when it will come in contact with phospholipid membrane.[15-17]

Ebbesen also reported caudad progression of icterus corresponds with an increasing bilirubin concentration. The same relationship exists in all infants except in small premature infants in whom it would have been reasonable to measure serum bilirubin when icterus had reached the area below umbilicus (dermal Zone III).[18]

Knudsen *et al*. studied cephalocaudal progression of jaundice in newborns admitted to neonatal intensive care units and confirmed the presence of the same. They found that significant correlation with serum bilirubin in female compared to males. Females have slightly lower albumin concentration than males and the reserve albumin concentration for binding may be slightly low in female, however in present study statistical analysis for correlation of serum bilirubin in different dermal zones showing insignificance ($P > 0.05$).[18]

The present study confirms the correlation of serum bilirubin with the progression of icterus but in low birth weight babies it would have been reasonable to measure serum bilirubin when icterus reaches the area below the umbilicus. Dermal zone assessment is not meant to replace assessment of serum bilirubin it might be helpful in those peripheral hospitals where round clock serum bilirubin measurement is not available so that early institution of therapy is possible in without waiting for laboratory confirmation.

CONCLUSION

A reliable association is noted between serum bilirubin and cephalocaudal progression of dermal icterus. The association holds true for lower bilirubin (dermal Zones I-III) level with the rise in bilirubin beyond dermal zone III serum bilirubin estimation is mandatory.

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