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CROSS-SECTIONAL STUDY TO COMPARE KRAMER'S AND MODIFIED KRAMER'S SCALES IN PREDICTING TOTAL SERUM BILIRUBIN LEVELS IN TERM NEONATES

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ABSTRACT Neonatal jaundice is common, but delayed recognition of significant hyperbilirubinemia may result in acute bilirubin encephalopathy and kernicterus. This hospital-based cross-sectional diagnostic accuracy study compared conventional Kramer's method with Modified Kramer's method for estimating total serum bilirubin (TSB) and assessed their potential to reduce blood sampling. One hundred and sixty-five healthy term neonates with visible jaundice, gestational age ≥37 weeks and birth weight >2500 g were enrolled over 18 months. Neonates with prior phototherapy, congenital anomalies, illness or features suggestive of cholestasis were excluded. Each neonate was assessed using both clinical methods under natural daylight, followed by serum bilirubin estimation. Correlation, agreement, paired comparisons and diagnostic performance were assessed using STATA version 14. Significant hyperbilirubinemia (TSB ≥15 mg/dL) was present in 25 (15.15%) neonates. Kramer zone 3 and Modified Kramer zone 3 were the most frequent categories. Kramer's method showed a strong correlation with TSB (r=0.914, p<0.001), while Modified Kramer's method showed a slightly stronger correlation (r=0.938, p<0.001). Estimates within 2 mg/dL of measured TSB were observed in 86.06% and 89.70% of neonates, respectively. For significant hyperbilirubinemia, Modified Kramer's method demonstrated sensitivity of 96.00%, specificity of 97.14%, positive predictive value of 85.71%, negative predictive value of 99.27% and accuracy of 96.97%, compared with 92.00%, 95.71%, 79.31%, 98.53% and 95.15%, respectively, for conventional Kramer's method. Serum bilirubin testing was indicated in 35.76% with Modified Kramer's method versus 43.64% with Kramer's method. Differences in detection of significant hyperbilirubinemia and reduction in blood sampling were not statistically significant. Modified Kramer's method may therefore be a useful bedside screening approach, while serum bilirubin remains necessary for definitive assessment and treatment decisions.

KEYWORDS : Neonatal Jaundice, Hyperbilirubinemia, Kramer's Method, Modified Kramer's Method, Total Serum Bilirubin, Diagnostic Accuracy, Neonatal Screening

INTRODUCTION

Neonatal jaundice is one of the most frequent clinical findings during the neonatal period and is usually caused by increased bilirubin levels. Although most neonatal jaundice is physiological and self-limiting, failure to recognize significant hyperbilirubinemia can lead to acute bilirubin encephalopathy, kernicterus and permanent neurological impairment. The burden is particularly important in settings where access to laboratory testing and specialized neonatal care is variable.

Clinical visual assessment remains attractive because it is rapid, inexpensive and available at the bedside. Kramer described the cephalocaudal progression of dermal icterus, with extension of jaundice from the face towards the trunk and lower limbs associated with increasing bilirubin concentrations. However, visual estimation can be affected by lighting, skin pigmentation and observer experience. Modified Kramer's method incorporates both the extent and intensity of yellow discoloration and was developed to improve bedside estimation.

Total serum bilirubin is the laboratory reference for assessment of neonatal hyperbilirubinemia, but blood sampling is invasive and repeated testing may cause discomfort and increase workload. A reliable clinical screening method could help identify neonates who require laboratory confirmation while avoiding unnecessary sampling. The present study compared conventional Kramer's method with Modified Kramer's method in term neonates with visible jaundice, assessed their agreement with measured TSB, evaluated diagnostic performance for significant hyperbilirubinemia and examined their potential to reduce serum bilirubin sampling.

MATERIALS AND METHODS

This observational cross-sectional study was conducted in the Departments of Paediatrics and Neonatology, Travancore Medical College Hospital, Kollam, over 18 months after obtaining ethics committee clearance. The study population comprised healthy term neonates with clinical jaundice and birth weight >2500 g.

Neonates with gestational age ≥37 weeks and visible jaundice were eligible. Babies who had received phototherapy before enrolment, those with congenital anomalies, sick neonates and those with a clinical history suggestive of cholestasis were excluded. A sample size of 165 was calculated using previously reported specificity of Modified Kramer's method, with 95% confidence and the specified precision. Eligible babies were included consecutively using convenience sampling until the required sample size was reached. Written informed consent was obtained from the parents.

Maternal antenatal, birth and neonatal clinical information was collected using a structured proforma. Each eligible neonate underwent clinical assessment using conventional Kramer's scale and Modified Kramer's scale. Assessment was performed by inspection in a predetermined area under natural daylight. Conventional Kramer assessment recorded the cephalocaudal zone of jaundice. Modified Kramer assessment considered both the extent of jaundice and the intensity of discoloration, with the underlying colour described as lemon yellow for mild staining or orange-yellow for deeper staining. Serum total, direct and indirect bilirubin were estimated after clinical assessment.

The principal outcome was agreement between the clinical estimates and measured TSB. Significant hyperbilirubinemia was defined in the thesis as TSB ≥15 mg/dL. Diagnostic performance was assessed using sensitivity, specificity, positive predictive value, negative predictive value and overall accuracy. Correlation analysis, Bland–Altman agreement analysis, paired comparisons and comparison of blood-sampling recommendations were performed. Statistical analysis was carried out using STATA version 14. Written parental consent and institutional ethics clearance were obtained before enrolment, and confidentiality of participant information was maintained.

RESULTS

A total of 165 term neonates with visible jaundice were included. Most assessments were performed after 48 hours of life, with 43.64% assessed at ≥72 hours and 42.42% at 48–71 hours. There was an almost equal sex distribution, with 50.30% males and 49.70% females. Most neonates had birth weight between 2501 and 2999 g, and 36.36% had gestational age of 39 weeks or more. All mothers had registered antenatal care. Caesarean delivery accounted for 58.79% of births. ABO incompatibility was more frequent than Rh incompatibility.

Kramer zone 3 was the most frequent conventional clinical category, occurring in 33.33% of neonates. Modified Kramer zone 3 was also the

most frequent category, accounting for 37.58%. Total serum bilirubin was below 10 mg/dL in 44.24% of neonates. Significant hyperbilirubinemia (TSB ≥15 mg/dL) was present in 25 (15.15%) neonates. Direct bilirubin values were within the normal range in the study population.

Kramer's method demonstrated a strong positive correlation with measured TSB ($r=0.914$, $p<0.001$). The mean estimated bilirubin was 10.48 mg/dL compared with a mean actual TSB of 10.83 mg/dL, with a mean difference of −0.35 mg/dL. Estimates were within 2 mg/dL of measured TSB in 86.06% of neonates.

Modified Kramer's method demonstrated a slightly stronger correlation with TSB ($r=0.938$, $p<0.001$). Estimates were within 2 mg/dL of measured TSB in 89.70% of neonates. For significant hyperbilirubinemia, conventional Kramer's method identified 23 of 25 cases, with two false-negative results. Modified Kramer's method identified 24 of 25 cases, with one false-negative result. Sensitivity, specificity, positive predictive value, negative predictive value and accuracy were 92.00%, 95.71%, 79.31%, 98.53% and 95.15%, respectively, for Kramer's method, and 96.00%, 97.14%, 85.71%, 99.27% and 96.97%, respectively, for Modified Kramer's method.

The difference in identification of significant hyperbilirubinemia was not statistically significant ($p=0.500$). Serum bilirubin sampling was indicated in 72 (43.64%) neonates by Kramer's method and in 59 (35.76%) by Modified Kramer's method. Thus, Modified Kramer's method classified 106 (64.24%) neonates as not requiring serum bilirubin sampling compared with 93 (56.36%) using conventional Kramer's method. The difference was not statistically significant ($p=0.108$). For predicting the need for sampling, Modified Kramer's method showed sensitivity of 96%, specificity of 75%, positive predictive value of 40.68%, negative predictive value of 99.06% and accuracy of 78.18%.

Table 1: Diagnostic Performance For Significant Hyperbilirubinemia

Parameter	Kramer	Modified Kramer
Sensitivity (%)	92.00	96.00
Specificity (%)	95.71	97.14
PPV (%)	79.31	85.71
NPV (%)	98.53	99.27
Accuracy (%)	95.15	96.97

PPV: positive predictive value; NPV: negative predictive value.

DISCUSSION

The study demonstrates that both conventional Kramer's and Modified Kramer's methods have a strong relationship with laboratory-measured TSB in healthy term neonates with visible jaundice. Modified Kramer's method showed a modest improvement in correlation, agreement within 2 mg/dL and diagnostic performance for significant hyperbilirubinemia. These findings are consistent with the rationale for incorporating intensity in addition to the cephalocaudal distribution of jaundice.

The predominance of intermediate Kramer zones is compatible with the expected cephalocaudal progression of neonatal jaundice. The study population was restricted to term neonates and excluded infants with suspected cholestasis or significant illness, thereby reducing heterogeneity and allowing assessment of clinical visual methods in a relatively healthy population. The greater frequency of ABO than Rh incompatibility was also observed in the study.

An important finding was the high diagnostic performance of both methods. Conventional Kramer's method identified 92% of neonates with significant hyperbilirubinemia, while Modified Kramer's method identified 96%. Although the modified method missed fewer cases and had higher sensitivity, specificity and predictive values, the difference was not statistically significant. Therefore, the observed numerical advantage should be interpreted as a potential improvement rather than proof of superiority.

The potential reduction in blood sampling is clinically relevant. Modified Kramer's method indicated serum bilirubin testing in 35.76% compared with 43.64% using conventional Kramer's method. Despite fewer recommended blood tests, the modified method detected one additional case of significant hyperbilirubinemia. However, the reduction was not statistically significant. These findings suggest that refinement of visual assessment may improve efficiency but cannot replace laboratory confirmation.

The results are broadly consistent with previous work cited in the thesis. Bansal et al. reported improved clinical assessment with Modified Kramer's method compared with the conventional scale. Other studies have shown that visual assessment correlates with bilirubin levels but may still show clinically relevant individual differences. Studies examining skin pigmentation and observer-related variation have also demonstrated that the reliability of visual assessment is context dependent. These factors support the use of standardized lighting, appropriate training and laboratory confirmation when indicated.

The clinical implication is that Modified Kramer's method can function as a bedside screening tool, especially where immediate access to transcutaneous or serum bilirubin measurement is limited. Nevertheless, visual assessment should not be considered a substitute for TSB when treatment decisions depend on an exact bilirubin concentration. The American Academy of Pediatrics guidance cited in the thesis emphasizes laboratory bilirubin measurement for definitive management decisions.

This study has several limitations. It was conducted at a single institution and used convenience sampling, which may limit generalizability. Only term neonates with visible jaundice and birth weight above 2500 g were included, so the findings cannot automatically be extended to preterm infants, low-birth-weight infants or neonates without clinically apparent jaundice. Inter-observer variability was not assessed. In addition, the relatively small number of neonates with significant hyperbilirubinemia limits precision when comparing diagnostic performance. Further multicentre studies with standardized observers and assessment of inter-observer reliability would help establish the reproducibility of Modified Kramer's method.

The practical value of a bedside assessment is greatest when it is used within a clear screening pathway. In the present study, Modified Kramer's method identified almost all neonates with significant hyperbilirubinemia while recommending fewer serum bilirubin measurements than conventional Kramer's assessment. At the same time, one neonate with significant hyperbilirubinemia was missed by the modified method. This reinforces the importance of clinical vigilance and follow-up even when the bedside assessment appears reassuring. The study therefore supports Modified Kramer's method as an adjunct to clinical screening rather than as a stand-alone diagnostic test. Its usefulness may be particularly relevant in settings where laboratory resources are limited, provided that infants with higher-risk clinical findings or concerning bilirubin estimates undergo serum bilirubin measurement.

CONCLUSIONS

Both conventional Kramer's and Modified Kramer's methods demonstrated strong correlation with measured total serum bilirubin and good diagnostic performance for significant hyperbilirubinemia in healthy term neonates with visible jaundice. Modified Kramer's method showed a modest numerical improvement in correlation, agreement and diagnostic performance and classified a greater proportion of neonates as not requiring serum bilirubin sampling. However, the differences in detection of significant hyperbilirubinemia and reduction in blood sampling were not statistically significant. Modified Kramer's method may therefore be considered a useful bedside screening tool, particularly in resource-constrained settings, but serum bilirubin estimation remains essential for definitive diagnosis and treatment decisions.

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