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Research Article

Validity of Kramer Scale in Neonatal Hyperbilirubinemia

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Abstract

Introduction: Jaundice refers to the yellow discoloration of sclera, skin and mucous membranes. It is a common problem that is faced during the first week of life by nearly every neonate. It is important to determine whether the clinical examination can be used reliably as a clinical screening tool for the diagnosis of neonatal jaundice. The diagnostic accuracy of Kramer's rule was compared to venous method in this study in order to provide less invasive, time consuming and less painful method of measuring neonatal hyperbilirubinemia.

Objective: To determine the diagnostic accuracy of Kramer's rule of assessing neonatal hyperbilirubinemia taking serum bilirubin as "Gold standard".

Setting: New-born nursery at Paediatric Unit, Liaquat University Hospital, Hyderabad, Sindh.

Design: Cross sectional validation study.

Subject and Methods: A total of 317 neonates coming under inclusion criteria presenting at new-born nursery were examined. First, baby is undressed and clinical assessment of jaundice done. Then the venous blood sample was collected for serum bilirubin level and sent to diagnostic lab. Data was collected on predetermined pro-forma.

Results: The average age of the neonate was 3.51±1.55 days. Sensitivity, specificity, positive predicted value, negative predicted value and accuracy of Kramer's Rule in detection of neonatal hyperbilirubinemia was 90.7%, 80.5%, 88%, 84.6% and 86.75% respectively.

Conclusion: Our study demonstrated that the Kramer's scale could be better choice for detection and screening of neonatal hyperbilirubinemia. It is a non-invasive and quick method that can avoid babies from getting a skin infection or other complications related to blood sampling.

Keywords: Jaundice; Kramer's rule; Neonatal hyperbilirubinemia

Introduction

Jaundice refers to the yellow discoloration of sclera, skin and mucous membranes [1]. It is a common finding present during the first week of life in nearly all the neonates [2]. Neonatal jaundice is primarily of two types: Physiological and Pathological. The discoloration of skin usually results from the deposition of excess quantities of unconjugated bilirubin pigment in the skin. The term "Kernicterus" describes a deposition of unconjugated bilirubin in the brain tissues which causes permanent neurological damage [3]. Therefore, early detection and treatment is necessary for the prevention of mortality and morbidities related to this problem [4].

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Throughout the world, the development of neonatal hyperbilirubinemia to a certain degree is an unpreventable condition in 60-80% of the neonates [4,5]. A locally conducted survey estimated the incidence of neonatal jaundice in a poor urban community in Karachi, with an overall detection rate of hyperbilirubinemia (bilirubin >5mg/dl) among 1690 new-borns in 39.7/1000 live births [5]. The burden of neonatal jaundice is more in South Asian countries as compared to developed countries [6].

For the diagnosis and monitoring of neonatal jaundice, intravenous blood samples are drawn for measuring serum bilirubin level which causes trauma and discomfort to the patient and the parents. There are other issues such as difficult venous access, multiple pricks or skin infections at sampling sites [7].

In developing countries like Pakistan there is a significantly higher number of births taking place at home, alongside decreased awareness and health seeking behaviours usually characterized by seeking home based or local treatments before coming to a proper health facility. Even if neonates present in reasonable time at a health facility, health care providers are usually unable to provide effective treatment due to lack of rapid serum bilirubin testing and sub-optimal phototherapy methods [8]. In these circumstances, the Kramer's rule offers multiple benefits in assessing jaundice in a neonates; it is a safe, easy and non-invasive visual method of assessing levels of hyperbilirubinemia.

Kramer's rule is based on observing the progression of jaundice from head to toe and estimating serum bilirubin levels. Kramer's scale correlates serum bilirubin concentrations to specific dermal zones: (1) Head and neck, (2) Upper trunk, (3) Lower trunk and thigh, (4) Arms and legs, (5) Hands and feet. Lower levels coincide with discoloration over head and neck and higher levels with discoloration over hands and feet [9].

Older studies has detected sensitivity value of Kramer's rule 82.4%, specificity of 81.8%, positive predictive value of 32.8%, negative predictive value 97.6% [10] Another study quotes sensitivity value of 76.92%, a specificity value of 89.47% [11].

A recent study recommended the use of the Kramer's method in neonatal units in Hospitals, preferably in those lacking transcutaneous bilirubin meters and particularly where quick assessment is needed for rapid clinical decision-making [12]. However, some studies have suggested that clinical examination with visual assessment for jaundice in new-borns is neither reliable nor accurate [13]. Therefore, a decision to perform serum bilirubin testing should be based on consideration of any additional factors present [13].

Currently, limited data is available in our region. The relationship between clinical appearance of jaundice and serum bilirubin measurement is not found to be consistent in various studies [12,13]. It is therefore very important to determine whether the clinical examination can be used reliably as a clinical screening tool for the diagnosis of neonatal jaundice. In our study we have tried to check the diagnostic accuracy of Kramer's rule (clinical examination) and have compared it to venous sampling test (method) result in order to prove and substantiate the hypothesis that less invasive, quick and less painful method of measuring neonatal hyperbilirubinemia can be achieved by simple clinical examination and correlating it with various levels of jaundice (Kramer's method). This will enable quicker decision making by health professional and decrease distress for babies and parents.

Material and Methods

Study design: Cross sectional validation study.

Study setting: New-born nursery at Paediatric Unit, Liaquat University Hospital, Hyderabad, Sindh.

Duration of study: 2-years.

Sample size: Result of previously published reports as a reference taking sensitivity value of 76.92%, a specificity value of 89.47% [1] prevalence 60% [4,5] and taking a confidence interval level of 95%, margin of error of 6%, the sample size was calculated to be 317 by sample size calculator.

Sampling technique: Non-probability consecutive sampling.

Inclusion criteria: All neonates including early term, full term and late term of both genders presenting with suspected jaundice at 0-7 days at New-born Nursery Paediatric Unit 1, Liaquat University Hospital.

Exclusion Criteria: Babies with established direct hyperbilirubinemia, septicaemia, major congenital/ gastrointestinal malformations and those started on phototherapy.

Data Collection Procedure

All the neonates coming under inclusion criteria presenting at new-born nursery was examined. Written and verbal informed parental consent for venous sampling was taken. First baby is undressed and clinical assessment of jaundice is done under fluorescent light augmented by natural sunlight during daylight hours or only under fluorescent light during night time, by blanching the baby's skin with thumb pressure and observing the underlying skin colour. The underlying skin colour changes from a lemon yellow to a deeper orange yellow. Each neonate included in study was given a score of 1-5 according to visual assessment by Kramer's rule by the researcher. Jaundice noted on head and neck was scored as 1, upper trunk neck was scored 2, lower trunk and thighs neck was scored 3, arms, legs, below knee neck was scored 4, hands and feet including palms and soles neck was scored 5. The venous blood sample was collected for serum bilirubin concentration with the help of an experienced paediatric nurse. Blood samples were sent to Diagnostic and Research Laboratory, Hyderabad and results collected. The data was collected on a predetermined pro-forma and information including demographical details (age, gender, weight, and gestational age), methods of delivery, and mode of feeding was recorded.

Data was the analysed using SPSS Version 23. Qualitative variables of this study i.e. gender, clinical presentation, mode of delivery, mode of feeding outcome sensitivity, specificity, positive predictive value and negative predictive value were reported as frequencies and percentages. Quantitative variables: Age, Birth weight, Kramer's rule score, and Serum Bilirubin level were described using either Mean and Standard Deviation or Median and Interquartile Range depending on the normality of data. The data was stratified according to gestational age, birth weight and gender to assess for any potential confounders or effect modifiers. Post stratification 'Chi square' test was used and the diagnostic accuracy was computed. It was considered significant at <0.05 value.

Results

A total of 317 neonates were included in this study. The average age of the neonate was 3.51±1.55 days. There were

169(53.31%) male and 148(46.69%) females. Regarding clinical presentation, 49.21% had a dark skin colour, while 50.79% had white collared skin. The gestational age of 40.38% of the respondents was early term, 49.84% full term and 9.78% were late-term. There were 56.67% neonates with vaginal delivered and 43.35% caesarean section. Out of 317 neonates, 47.32% were breast feeding and 52.28% were top fed.

The sensitivity, specificity, positive predicted value, negative predicted value and accuracy of Kramer's rule in detection of neonatal hyperbilirubinemia was 90.7%, 80.5%, 88%, 84.6% and 86.75% respectively as shown in Tables 1-9. Stratification analysis was performed and that showed a diagnostic accuracy of Kramer's rule above 80% in all stratified groups accept late term neonate as shown in table 6 to 9.

Table 1: Descriptive Sstatistics of Neonates.

Variables	Mean	95% Confidence Interval for Mean	
		Lower Bound	Upper Bound
Age (days)	3.51±1.55	3.34	3.68
Birth Weight (kg)	2.53±0.23	2.50	2.551
Kramer's rule score	1.37±0.48	1.32	1.42
Serum Bilirubin (mg/dl)	6.67±3.01	6.34	7.01

Table 2: Diagnostic accuracy of kramer's rule of assessing neonatal hyperbilirubinemia taking serum bilirubin as gold standard n=317.

KRAMER'S RULE	Total serum bilirubin		Total
	Positive	Negative	
Positive (Score≥2)	176 [TP]	24 [FP]	200(63.1%)
Negative (Score<2)	18 [FN]	99 [TN]	117(36.9%)
Total	194(61.2%)	122(38.8%)	317
Sensitivity	=90.7%		
Specificity	=80.5%		
PPV	=88.0%		
NPV	=84.6%		
Accuracy	=86.75%		

Table 3: Diagnostic accuracy of kramer's rule of assessing neonatal hyperbilirubinemia taking serum bilirubin as gold standard for male n=169.

KRAMER'S RULE	Total serum bilirubin		Total
	Positive	Negative	
Positive (Score≥2)	93	13	106
Negative (Score<2)	10	53	63
Total	103	66	169
Sensitivity	=90.3%		
Specificity	=80.3%		
PPV	=87.7%		
NPV	=84.1%		
Accuracy	=86.4%		

Table 4: Diagnostic accuracy of kramer's rule of assessing neonatal hyperbilirubinemia taking serum bilirubin as gold strandard for female.

KRAMER'S RULE	Total serum bilirubin		Total
	Positive	Negative	
Positive (Score≥2)	83	11	94
Negative (Score<2)	8	46	54
Total	91	57	148
Sensitivity	=91.2%		
Specificity	=80.7%		
PPV	=88.3%		
NPV	=85.2%		
Accuracy	=87.2%		

Table 5: Diagnostic accuracy of kramer's rule of assessing neonatal hyperbilirubinemia taking serum bilirubin as gold standard for early term neonate.

KRAMER'S RULE	Total serum bilirubin		Total
	Positive	Negative	
Positive (Score≥2)	69	14	83
Negative (Score<2)	1	44	45
Total	70	58	128
Sensitivity	=98.6%		
Specificity	=75.9%		
PPV	=83.1%		
NPV	=97.8%		
Accuracy	=88.2%		

Table 6: Diagnostic accuracy of kramer's rule of assessing neonatal hyperbilirubinemia taking serum bilirubin as gold strandard for full term.

KRAMER'S RULE	Total serum bilirubin		Total
	Positive	Negative	
Positive (Score≥2)	86	9	95
Negative (Score<2)	10	53	63
Total	96	62	158
Sensitivity	=86.6%		
Specificity	=85.5%		
PPV	=90.5%		
NPV	=84.1%		
Accuracy	=87.9%		

Table 7: Diagnostic accuracy of kramer's rule of assessing neonatal hyperbilirubinemia taking serum bilirubin as gold standard for later term.

KRAMER'S RULE	Total serum bilirubin		Total
	Positive	Negative	
Positive (Score≥2)	21	1	22
Negative (Score<2)	7	2	22
Total	28	3	31
Sensitivity	=75.0%		
Specificity	=66.7%		
PPV	=60.8%		
NPV	=22.2%		
Accuracy	=71.2%		

Table 8: Diagnostic accuracy of kramer's rule of assessing neonatal hyperbilirubinemia taking serum bilirubin as gold standard for ≤2.5kg birth weight.

KRAMER'S RULE	Total serum bilirubin		Total
	Positive	Negative	
Positive (Score≥2)	105	12	117
Negative (Score<2)	10	62	72
Total	115	74	189
Sensitivity	=91.3%		
Specificity	=83.3%		
PPV	=89.7%		
NPV	=86.1%		
Accuracy	=88.4%		

Table 9: Diagnostic accuracy of kramer's rule of assessing neonatal hyperbilirubinemia taking serum bilirubin as gold standard for >2.5kg birth weight.

KRAMER'S RULE	Total serum bilirubin		Total
	Positive	Negative	
Positive (Score<:2)	71	12	83
Negative (Score<2)	8	37	45
Total	79	49	128
Sensitivity	=89.9%		
Specificity	=75.5%		
PPV	=85.5%		
NPV	=82.2%		
Accuracy	=84.3%		

Discussion

The neonatal hyperbilirubinemia has always been a matter of concern for paediatricians worldwide. Visual examination by Kramer's scale has been used for many decades for screening of hyperbilirubinemia in new-borns. Being non-invasive and cost effective evaluation method, it is of valuable assistance to health personnel where laboratory facilities are not readily available [14]. With introduction of measuring serum bilirubin in the diagnosis of hyperbilirubinemia, babies were being pricked multiple times to check for variable levels of serum bilirubin for contant observation and management of the patients. This not only adds to worry and stress to parents but also causes pain and blood loss for babies. Transcutaneous bilirubinometry has come a long way as an effective tool for assessing bilirubin levels in new-borns since its introduction, approximately 4 decades ago.

In new-borns, Knudsen explained that there was a cephalocaudal progression of jaundice which is apparently related to the conformational changes in the newly formed bilirubin-albumin complexes [15]. Another reason attributed to this direction of progression, is the relative thickness of skin at various parts with the skin being the thinnest at face and thicker over the palms and soles. In the case of preterm babies, as the skin is relatively thinner, jaundice occurs even at lower serum bilirubin levels. With increase in the gestational maturity and postnatal age, this cephalocaudal colour difference is found to decreases.

In present study, the average age of the neonates was 3.51±1.55 days. There were 53.31% males and 46.69% females. The 56.67% neonates were born with vaginal delivery and 43.35% with caesarean section. In Varughese study, the males were 54.4% while female babies were 45.6%. Out of 450 babies, 65.1% babies were delivered by vaginal delivery, 5.1% by instrumental delivery and 29.8% were delivered by Caesarean section [16].

There have been differences in opinions among many paediatricians regarding the usefulness of the Kramer's scale. It is true that in poor resource settings, Kramer's scale continues to be effective in diagnosing significant hyperbilirubinemia, if examined by trained professional [17,18]. In healthy term babies, hyperbilirubinemia can be safely ruled out by visual assessment if jaundice does not reach the abdomen or the extremities (Kramer zones 1 and 2) [19].

In our study, sensitivity, specificity and accuracy of Kramer's rule in detection of neonatal hyperbilirubinemia was 90.7%, 80.5%, and 86.75%, respectively. Older studies have detected sensitivity of 82.4%, specificity of 81.8%, positive predictive value of 32.8%, negative predictive value 97.6% [10]. Another study quotes sensitivity value of 76.92%, a specificity value of 89.47% [11] While Joan 'et al' have demonstrated the ineffectiveness of the Kramer scale as a screening instrument with sensitivity and specificity at less than 48 hours being 67% and 47% respectively and between 49-72 hours the sensitivity and specificity being 89% and 54% respectively [20].

A recent study recommended the use of the Kramer's method in neonatal units in hospitals where there was lack of transcutaneous bilirubin meters who required quick assessment for rapid clinical decision-making [12]. Another study suggested that clinical examination with visual assessment for jaundice in new-borns is neither reliable nor accurate. The decision to perform serum bilirubin testing should also be based on additional factors [13].

In Tikmani 'et al' study, there was a significant correlation between Kramer scores of ‡4 (progression of jaundice to the knees and more peripherally to hands and feet) as assessed by physicians at the primary health care level with total serum bilirubin levels of ‡15mg⁄dl (P-value) [5].

Parents should be educated about the consequences of severe hyperbilirubinemia and taught simple means to prevent it. Exclusive breast feeding without prolonged periods of fasting, and avoidance of supplementation with dextrose or water is some documented measures associated with lower serum bilirubin levels in new-borns [21]. Pathological neonatal hyperbilirubinemia remains a major problem in developing countries such as Pakistan, where the burden goes largely unrecognized and unaddressed. Community-based interventions remain the most important avenue for any service delivery to underserved areas where mortality rates are highest.

Conclusion

In our study it was observed that Kramer's scale could be better and non-invasive choice to detect neonatal hyperbilirubinemia. Being simple clinical tool it not only avoids babies from getting a skin prick for blood sampling but also prevent associated complications such as infection, pain and psychological concerns. In settings where transcutaneous bilirubinometry is not feasible, it is better to screen for jaundice using Kramer's scale rather than estimating serum bilirubin values in all babies. In our opinion, the Kramer's scale is simple, reliable tool for clinical assessment of hyperbilirubinemia especially in remote facilities or under developed regions.

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