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Correlation of Clinical Assessment of Jaundice with Total Serum Bilirubin in Neonates: Hospital-Based Cross-Sectional Study

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Abstract:-

➢ ***Introduction:***

Neonatal jaundice is a common cause of admission in the neonatal period. Early diagnosis and treatment of neonatal jaundice prevent the bilirubin encephalopathy. There are various methods for the estimation of neonatal jaundice. Clinical assessment of neonatal jaundice can aid in the diagnosis of neonatal jaundice in low-resource settings and refer to the higher center for those who require treatment. This study aims to understand the relation between clinical assessment of jaundice and total serum bilirubin in neonates and to know the risk factors of neonatal jaundice.

➢ ***Methods:***

The Clinical assessment of jaundice by Kramers scale can be used to assess the level of jaundice and know the progression of jaundice.

➢ ***Results:***

This shows a significant positive relation between clinical assessment of jaundice and serum bilirubin level.

➢ ***Conclusions:***

The study findings showed that clinical assessment of jaundice was comparable with the serum bilirubin. Clinical assessment of jaundice by Kramer‟ 's scale can be used to assess the level of jaundice and know the progression of jaundice.

Keywords:- *Bilirubin, Jaundice, Kramers Scale, Neonate.*

I. INTRODUCTION

In French, “Juan” means yellow and the word jaundice was coined from there. It is a yellowish discoloration of the sclera and the body due to the deposition of bilirubin pigment in connective tissue.[1] Out of total newborns, around 8-11% develop hyperbilirubinemia requiring admission. When the total serum bilirubin rises above the 95th percentile for age, it falls in a high-risk zone. In the early neonatal period, it is considered a significant hyperbilirubinemia.[2,3] Neonatal hyperbilirubinemia is one of the common morbidities in newborn babies. Jaundice occurs more in preterm babies (80%) than in term babies (60%) in the early neonatal period.[4]

Hyperbilirubinemia means yellowish discoloration of the sclera, skin, and mucosa with an elevated concentration of serum bilirubin. Newborns appear jaundiced when bilirubin is more than 7mg/dl.[5] For the vast majority of these newborns increased total serum bilirubin (TSB) levels are benign and transitory with only 5% reaching levels that require treatment.[6,7] The red blood cells life span is only around 60 days in term neonates while it is 120 days in adults. It is one of the important causes of increased bilirubin in neonates than in adults[8,9] Neonatal jaundice is invariably present worldwide in all ethnic groups. It is the most common condition requiring evaluation and treatment in newborns.[10] More than 1 million babies develop severe neonatal jaundice worldwide every year and some of them also suffer from bilirubin encephalopathy. Most of these cases are from sub-Saharan Africa and South Asia.[11]

Elevation of bilirubin in neonates can lead to kernicterus, acute bilirubin encephalopathy, or chronic bilirubin encephalopathy. They have features like focal neurological deficits, neurobehavioral problems, and lower intelligence. Kernicterus is a neurological syndrome caused by the deposition of unconjugated bilirubin in the basal ganglia and nuclei of the brain stem.[12] Severe neonatal jaundice leads to acute bilirubin encephalopathy or kernicterus with a significant risk of neonatal mortality and long-term neurological damage such as cerebral palsy, sensory neural hearing loss, intellectual difficulties, or gross developmental delays.[13] High total serum bilirubin over critical level, crosses the blood-brain barrier. So, early identification and proper management are of great value in preventing bilirubin encephalopathy.[14]

Bilirubin can be estimated by using invasive techniques and non-invasive techniques. The invasive technique involves the measurement of urine urobilinogen and serum bilirubin levels in the blood. Noninvasive techniques include the assessment of neonatal jaundice visually by Kramer's rule and by using a transcutaneous bilirubinometer.[15]

There is a cephalocaudal progression of jaundice due to maximal perfusion of the face, then the trunk, and lastly the limbs. Dr. Kramer introduced criteria to assess neonatal jaundice visually in 1969. The scale is based on a cephalocaudal progression of jaundice. Jaundice progresses in a cephalocaudal manner as it starts from the face, then to trunk and extremities. Kramer formulated 5 zones of cephalocaudal progression of jaundice with zone 1 (bilirubin

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≤ 5 mg/dl), zone 2 (bilirubin 5-10 mg/dl), zone 3 (bilirubin 10-12mg/dl), zone 4 (bilirubin 12-15 mg/dl), zone 5 (bilirubin >15 mg/dl)[16]

Various risk factors were identified for neonatal jaundice. Exclusive breastfeeding, severe jaundice in previous siblings, prematurity, cephalhematoma, male sex, and normal vaginal delivery are risk factors for developing neonatal jaundice.[17-20]

The dermal zone method of estimating serum bilirubin concentration might be a useful aid in settings where accurate serum bilirubin determination is difficult to obtain frequently in newborns. In low-income countries like Nepal, frequent assessment of serum bilirubin levels may cause unnecessary trauma to the infants and anxiety to the family and it also increases cost to the family. This study helps to understand whether the clinical assessment of jaundice by Kramer‟s rule could serve as an initial step for diagnosing and categorizing neonatal jaundice. So, early intervention can be taken to reduce the risk of neurotoxicity due to bilirubin encephalopathy. The decision on whether to draw blood for measurement of bilirubin can be made clinically which prevents many unnecessary skin punctures and burdens. In rural areas of our country where laboratory setup is not available clinical methods of estimation of bilirubin levels in neonates done with adequate knowledge and practice can be helpful for early recognition of neonatal jaundice and can be referred to higher centers for those who require treatment.

II. METHODS

- Type of Study: Hospital-based cross-sectional study.
- Study Population: All neonates having jaundice presenting in the Pediatrics outpatient department (OPD), Neonatal Intensive Care Unit (NICU), neonatal ward, and postnatal care (PNC) ward of Nepal Medical College Teaching Hospital.
- Study period: 1 Year (August 2021 - July 2022)
- Sample size Considering correlation coefficient r=0.283 according to the study conducted by Varughese PM[36]

α: Threshold probability for rejecting the null hypothesis. Type I error rate = 0.05 at 95% confidence interval,

β: Probability of failing to reject null hypothesis under alternate hypothesis. Type II error rate = 0.2 at 80% power of study,

Standard normal deviate for $\alpha = Z\alpha = 1.9600$,
Standard normal deviate for $\beta = Z\beta = 0.8416$,

$C=0.5\times In[(1+r)/(1-r)]=0.5\times In[(1+0.283)/(1-0.283)] = 0.2909$

Total sample size $N = [(Z\alpha+Z\beta)/C]2+3 = [(1.96+0.84)/0.2909]2+3 = 96$

Ethical approval was obtained from the Nepal Medical College-Institutional Review Committee (NMC-IRC) 05-078 / 79. Written informed consent was taken from parents or local guardians of all neonates. They were informed about the study and the details of the process were explained to them. The patient was allowed to withdraw from the study at any time. All the information collected from the patient was kept confidential.

Kramer‟s rule can be used to assess the jaundice in neonates clinically before drawing the blood which minimizes unnecessary sampling and burden to the parents.

Statistical analysis; The data was entered in SPSS version 21 for analysis. The demographic variables were studied in the sample. The relationship between clinical assessment of jaundice and serum bilirubin is studied using ANOVA. A p-value of <0.05 was taken as significant.

The data was collected and compiled by the researcher. Afterward, the collected data was entered into a Microsoft Excel spreadsheet. The Statistical Package for Social Sciences (SPSS) 21 software was used for the analysis of data

III. RESULTS

In this study, a total of 104 neonates were enrolled as per inclusion criteria. The median age of the baby was 4.5 days ranging from 1-25 days. The mean gestational age was 38.53 ± 1.407 weeks. The mean birth weight was 3151.15 ± 520.81 grams.

Table 1: Descriptive Data

Kramer‟s scale	Number (n=104)	Mean of serum bilirubin (mg/dL)	Standard deviation	Minimum bilirubin (mg/dL)	Maximum bilirubin (mg/dL)
Zone 1	9	3.5778	1.09291	2.30	5.40
Zone 2	32	8.5188	2.01837	4.50	12.70
Zone 3	22	11.9027	1.57352	9.40	14.90
Zone 4	14	14.9143	2.06951	11.90	17.90
Zone 5	27	20.0741	2.19748	15.70	24.50
Total	104	12.6679	5.59833	2.30	24.50

IV. DISCUSSION

In the present study, the sample consisted of 104 neonates, belonging to age groups of 1-25 days (median age 4.5 days). Studies have shown that bilirubin concentration increases within the first 96-120 hours of birth, peaks on days 5 to 7, and then decreases. The subjects within the range of 1-25 days were included in the study.

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Gender and serum bilirubin In this study, out of the total 104 cases, 68 (65.4%) were male, and the remaining 36 (34.6%) were females. A study done by Maisels et al also identified male newborns had a higher risk of neonatal jaundice compared to females.[14] Varughese et al conducted a study on neonatal jaundice at a tertiary care center in south India for around 2 years. Out of 450 neonates, 54.4% were male babies in that study which showed more males than females with neonatal jaundice.[21] Similarly, a study done by Aprillia et al showed more incidence of neonatal jaundice in male babies than females which has 68.6% of males.[22] This signifies male gender has a higher risk of neonatal jaundice than the female gender.

Relation between clinical assessment of jaundice and total serum bilirubin ANOVA was applied to determine the relation between clinical assessment of jaundice using the Kramer scale and total serum bilirubin. The F-test was found to be statistically significant (P-value < 0.001) which shows a positive relation between clinical assessment of jaundice and serum bilirubin level.

The present study was also supported by Szabo et al in their study done in 69 subjects. The study was carried out in the maternity ward and the neonatal intermediate care unit of the University Hospital Zurich between 1 March 2002 and 28 February 2003. By Kramer‟s scale, ROC area was 0.73 for nurses and 0.70 for the primary investigator. The study showed the positive significance of Kramer‟s scale for the identification of jaundice and serum bilirubin.[23]

Similarly, Varughese et al conducted a prospective observational study on newborns with neonatal jaundice from November 2014 to June 2016 in a neonatal unit of a medical college hospital in South India. It showed a significant positive relation between Kramer‟ 's rule of assessment of jaundice correlated with total serum bilirubin at 24 hours whereas there was a weak correlation in 48 hours.[21]

A prospective study was done by Hatzenbuelher between September 2004 and March 2005 in a multiethnic population of infants presenting to three primary health-care clinics in Karachi, Pakistan. Primary health-care workers identified 1 to 20-day-old neonates with hyperbilirubinemia with 83.3% sensitivity and 50.5% specificity.[24]

Similar results were found in a cross-sectional descriptive study done by Aprillia et al on 102 neonates. The study showed that the sensitivity, specificity, and accuracy of the Kramer test were 76.92%, 89.47%, and 86.27% respectively which was good for determining jaundice among neonates.[22]

A cross-sectional study was conducted by Dionis et al at a hospital in Tanzania in 2022 on 315 neonates. The sensitivity and specificity of Kramer‟s method was 70.5% and 86.1% respectively. Similarly, the positive predictive value, negative predictive value, and diagnostic accuracy of Kramer‟s method were 89.8%, 62.6%, and 76.1% respectively. They concluded that Kramer‟s method has good predictive value.[25]

Mumtaz et al did a comparative cross-sectional study at a hospital in Pakistan in 2019 with over 300 neonates. The sensitivity and specificity of the Kramer‟s scale were 83.84% and 73.53% respectively for zone 1 to 3.[26]

Similarly, another cross-sectional study was conducted at Liaquat University Hospital over 2 years on 317 neonates with jaundice. They found that the sensitivity, specificity, positive predicted value, and negative predicted value of Kramer‟s method were 90.7%, 80.5%, 88%, and 84.6% respectively. The diagnostic accuracy of Kramer‟s method was 86.75%.[27]

However, Moyer VA et al demonstrated different results, where they showed that clinical examination of jaundice was not a reliable method. They concluded that the prediction of serum bilirubin concentration using clinical examination had poor accuracy.[28]

This difference could be attributed to variation in the sample, methodological differences, or publication bias. A limited sample size representing a small proportion of the Nepali population could be another limiting factor. Thus, the study emphasizes the importance of further research to explore the relationship between jaundice and risk factors, and the efficiency of Kramer‟s scale among large populations. I am grateful to my seniors and my colleagues for their suggestions and support they have extended to me during this study

V. LIMITATIONS

- This study was carried out in a small sample size, in a short period, and a single center only. A similar study can be replicated with a large sample size for a longer duration in multiple centers to draw a better and stronger conclusion.
- The risk factors can also be studied with a control group for better generalization of the result.

VI. CONCLUSIONS

The study findings showed that clinical assessment of jaundice was comparable with the serum bilirubin. Clinical assessment of jaundice by Kramer's scale can be used to assess the level of jaundice and know the progression of jaundice. Clinical assessment of jaundice by Kramer’s rule can be used in low-resource settings reliably to estimate the level of jaundice. Neonatal jaundice was more common in male gender and breastfed babies.

- Conflict of Interest: None

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