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Original Article

Study of Cord Blood Bilirubin Levels in a Tertiary Care Centre of Kumaun Region (Uttarakhand) India

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ABSTRACT
Jaundice in newborn is a very common problem. Neonatal hyper bilirubinemia (NH) may lead to kernicterus in otherwise healthy newborns. This can be easily prevented if excessive hyper bilirubinemia for age is promptly identified and appropriately treated. Newborns can be screened for severity of bilirubinemia before hospital discharge which may help in early detection of the newborns at risk for excessive hyper bilirubinemia during the first week of life. To determine the level of cord blood bilirubin in all healthy term new borns and asses its usefulness in predicting neonatal jaundice. Neonatal jaundice (NNJ) is an interesting, complicated and controversial clinical problem. It is a cause of concern for the parents as well as pediatricians. The concept of prediction of jaundice offers an attractive option to pick up babies at risk of neonatal hyper bilirubinemia. Physical examination is not a reliable measure of serum bilirubin. Under these circumstances it would be desirable to be able to predict the risk of jaundice, in order to implement early treatment and thereby minimize the risk of bilirubin dependent brain damage. Neonatal Hyper bilirubinemia has been defined as the bilirubin levels > 12.9 mg/dl in term babies and 15 mg/dl in preterm babies. Neonatal jaundice is visible manifestation in skin and sclera of elevated serum concentrations of bilirubin and this usually occurs in neonates if serum bilirubin level is >5 mg/dl. Most adults are jaundiced when total serum bilirubin (TSB) levels exceed 2.0 mg/dL. Kernicterus and near miss kernicterus are neonatal conditions that are associated with irreversible or reversible brain injury respectively. Concerns regarding jaundice have increased after reports of bilirubin encephalopathy occurring in healthy term infants without hemolysis. This study was conducted in 80 term newborns, a tertiary care center, Department of Pediatrics, Government medical college & Hospital, Haldwani Uttarakhand from July 2013 –Feb 2014. Serum bilirubin estimation was done in the Biochemistry department, Center lab of Government medical college, Haldwani (Formerly STM Haldwani) Uttarakhand. Serum bilirubin estimation was done by Diazo

method. All babies were classified into four groups depending on the UCS bilirubin levels <0.9 (group-I), 1.0-1.9 (group-II), 2.0-2.9 (group-III), >3 (group-IV). Serum bilirubin estimation was done after 72 hours of postnatal life. Babies were categorized according to the need for phototherapy. Statistical analyses of significance (chi-square) were applied and the predictive values (sensitivity, specificity, PPV, NPV) were calculated using the conventional formulae. Incidence of NNJ in our study is 14 %. Mean total bilirubin on third post natal day was 9.14 mg/dl. Using CBB level of ≥ 1.9 mg/dl as a cut-off, NNJ can be predicted with sensitivity of 92.8%, specificity of 83.7 %, and positive predictive value of 48.1 % and negative predictive value of 98.6 %. The Negative Predictive Value (98.6%) in the present study suggests that in healthy term babies (without RH and ABO incompatibility with Cord Blood Bilirubin ≤ 1.9 mg/dl) cord serum bilirubin can help to identify those newborns who are unlikely to require further evaluation and intervention. These newborns can be discharged with assurance to parents. Babies with CBB level ≥ 1.9 mg/dl should be followed more frequently.

Keywords: *Newborn, Neonate, Neonatal Jaundice, Cord blood bilirubin.*

INTRODUCTION

The word 'Jaundice' is derived from the French word 'Jaune' meaning yellow. Neonatal hyper bilirubinemia is a yellowing of the skin and other tissues of a newborn infant. In adults, jaundice is visible when serum bilirubin exceeds 2 mg/dl but in the newborn it is seen when the serum bilirubin exceeds 4 mg/dl. Unlike in children and adults where all jaundice is pathological, in the newborn most jaundice is physiological. [1, 2] Neonatal jaundice is one of the major causes of admission in newborn nurseries. Jaundice is observed during the 1st week of life in approximately 60% of term infants and 80% of preterm infants.[3,4] According to National Neonatal- Perinatal Database (NNPD) the incidence of neonatal hyperbilirubinemia in intramural live-births is 3.3% while in extramural admissions morbidity due to hyperbilirubinemia accounted for 22.1%.[5] Early discharge of healthy term newborns after delivery has become a common practice because of medical, social and economical reasons. The most common cause for readmission during the early neonatal period is hyperbilirubinemia. Such readmission, besides involving extra expenses for both family and the institution and also exposing a probably healthy new born to the hospital environment, brings emotional problems and risks to breast-feeding, and is one of the causes of early weaning.[6] Concern regarding early discharge and hyper bilirubinemia in new borns has led to frequent discussions and many controversies. Early hospital discharge has had the implication of reexamining the approach toward neonatal jaundice, now taking into consideration the bilirubin levels presented in the first 24–48 h of life as a means of predicting severe hyperbilirubinemia.[7,8] Thus, the investigation of parameters that might help the physician prevent the occurrence. In recent years many efforts have been made to identify infants likely to develop neonatal jaundice. Reliable strategies can reduce hospital stay for normal babies and identify significant hyper bilirubinemia that may happen in the future. Universal follow-up within 1–2 days of early discharge, umbilical cord bilirubin concentration at birth, routine pre-discharge serum bilirubin and transcutaneous bilirubin measurement, as well as the universal clinical assessment of risk factors of developing jaundice are various strategies to predict significant hyper bilirubinemia.[9] So that, it would be desirable to be able to predict the risk of jaundice in order to implement early treatment and thereby minimize the risk of bilirubin dependent brain damage.[10,11]

Christian Georg Schmorl coined the term kernicterus (jaundice of the nuclei), which has subsequently been used both to describe a pathoanatomical picture seen at autopsy in those who died, as well as a neurological syndrome in survivors of extreme jaundice. [12] In his landmark paper Schmorl described his findings from the autopsies of 280 neonates, of whom 120 were jaundiced at the time of death. In the majority of these cases (114/120), he found the brain to be diffusely yellow. [13] He noted that the intensity of

the brain colour paralleled that of the face, which is often the most intensely jaundiced part of an infant's body, as also described by Hervieux. In the brains that Schmorl examined, the jaundiced nuclei were very sharply demarcated and, therefore, contrasted clearly with the colour of the surrounding tissue. Because of this sharp demarcation and the predilection for staining of the nuclei, Schmorl proposed the term kernicterus. [14] He further suggested that the yellow colour was not simply attributable to saturation of the tissue with bile pigments, such as was the case (he believed) with eg, skin, but to binding of the bile pigments to specific structural elements in the tissue. Microscopic examination of the tissue supported this hypothesis. Some neurons in the nuclei were strongly coloured, while others had a pale yellow colour. These latter cells exhibited changes that suggested that they were in the process of dying. In 1847, Virchow suggested that the excessive destruction of red blood cells in the first week of life is the basic cause of jaundice. Molisan demonstrated by transfusion experiments that erythrocytes of new born break down twice as rapidly as compared to adults. [15]

Beneke in 1907, was the first to suggest that septicaemia might play an important role in icterus gravis neonatorum, and he theorized that the pigmentation of brain tissue was caused by a peculiar attraction of bile pigments to ganglion cells leading to their necrosis, damage to the ganglion cells by the bile salts which then became pigmented, or ischemic or the traumatic insult that allowed the cells to become pigmented. [16] As early as 1913, there were description of children who survived severe neonatal jaundice with resultant mental retardation and neuromuscular dysfunction, with the jaundice being considered the causal agent (Guthrie, 1913; Spiller, 1915).[17] Yippo, a great Finnish Pediatrician, was the first person to investigate extensively on neonatal jaundice. In a paper published in 1913, "zeitschrifit der kinderheilunde", he described the yellowish discolouration of the newborn and umbilical cords. He also proposed a theory that functional immaturity of liver prevented the excretion of all bilirubin that is formed, permitting some to re-enter the circulating blood. [18] In 1932, Diamond and colleagues recognized that generalized edema of the fetus (hydropsfetalis), icterus gravis and congenital anaemia of the new born were all in fact a part of single condition which they termed "isoimmunisation fetalis". In 1946, they introduced the technique of alternate removal and administration of blood for each transfusion by umbilical vein catheterization. Allen et al in 1950 showed effectiveness of exchange transfusion as a protection from kernicterus. [19] In 1951, Halbreent coined the term "Icterus precox" for jaundice developed within 24 hours of birth. [20]

MATERIAL AND METHODS

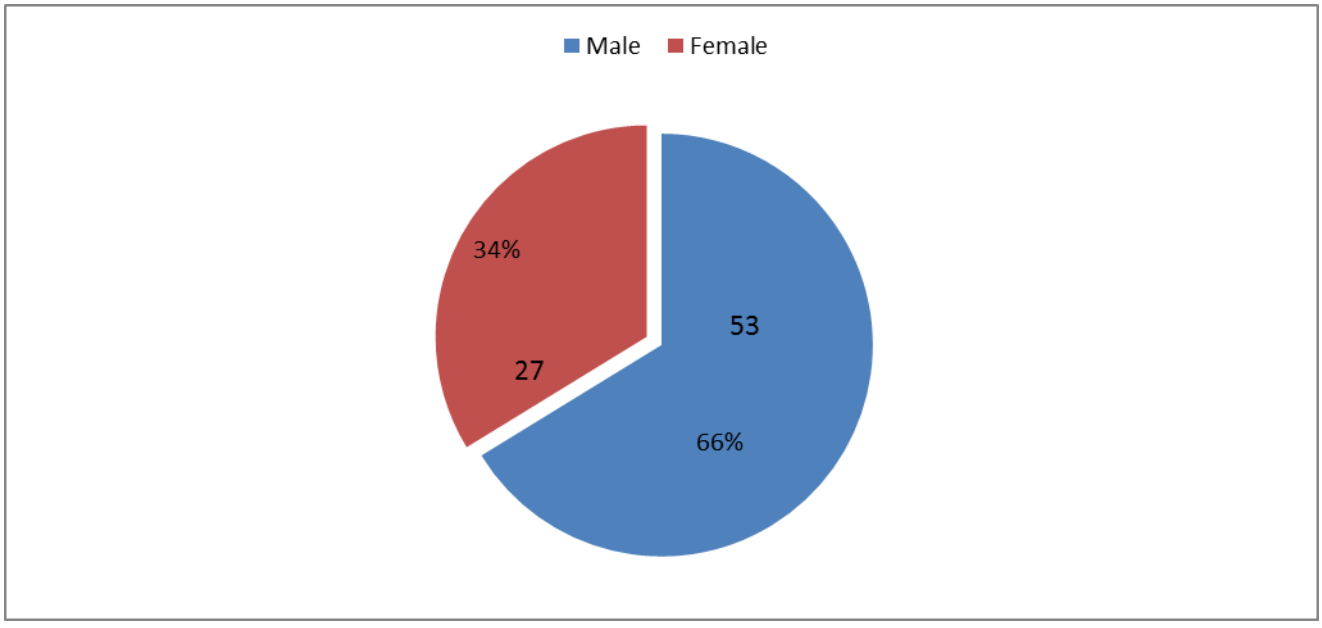
This study was conducted in 80 term newborns, a tertiary care center, Department of Pediatrics, Government medical college & Hospital, Haldwani Uttarakhand from July 2013 –Feb 2014. Serum bilirubin estimation was done at birth from cord blood and then at 72 hours of life from peripheral venous blood sample. A prospective cohort study was conducted in which the newborns were followed up clinically and by laboratory investigation during the period of their hospital stay. At the time of this study, neonates were observed for three days post-delivery period, prior to discharge. Inclusion Criteria was all full term neonates delivered by normal vaginal delivery (NVD) or lower segment caesarean section (LSCS) ,with birth weight >2.5 kg and no birth asphyxia. Cord blood samples for analysis of conjugated, unconjugated and total bilirubin levels were collected from all newborns that complied with the protocol inclusion criteria. These newborns were followed up for the 3-day period of their hospital stay. They were physically examined daily and also whenever necessary bilirubin levels were done. Values of bilirubin at third day were compared with those of cord blood bilirubin. In all cases the recommendation for phototherapy was followed according to the

schedule proposed by the AAP. 2 ml each of plain cord blood samples were collected from the umbilical cord and investigated for ABO Blood grouping and Rh typing, total and differential serum bilirubin assessment. 2 ml plain venous blood was collected from the baby after 72 hours and total and differential serum bilirubin were assessed. Blood collected was transported to laboratory within 2 hours of collection. Serum bilirubin estimation was done in the Biochemistry department, Center lab of Government medical college, Haldwani (Formerly STM Haldwani) Uttarakhand. Serum bilirubin estimation was done by Diazo method. All babies were classified into four groups depending on the UCS bilirubin levels <0.9 (group-I), 1.0-1.9 (group-II), 2.0-2.9 (group-III), >3 (group-IV). Serum bilirubin estimation was done after 72 hours of postnatal life. Babies were categorized according to the need for phototherapy. Statistical analysis of significance (chi-square) was applied and the predictive values (sensitivity, specificity, PPV, NPV) were calculated using the conventional formulae.

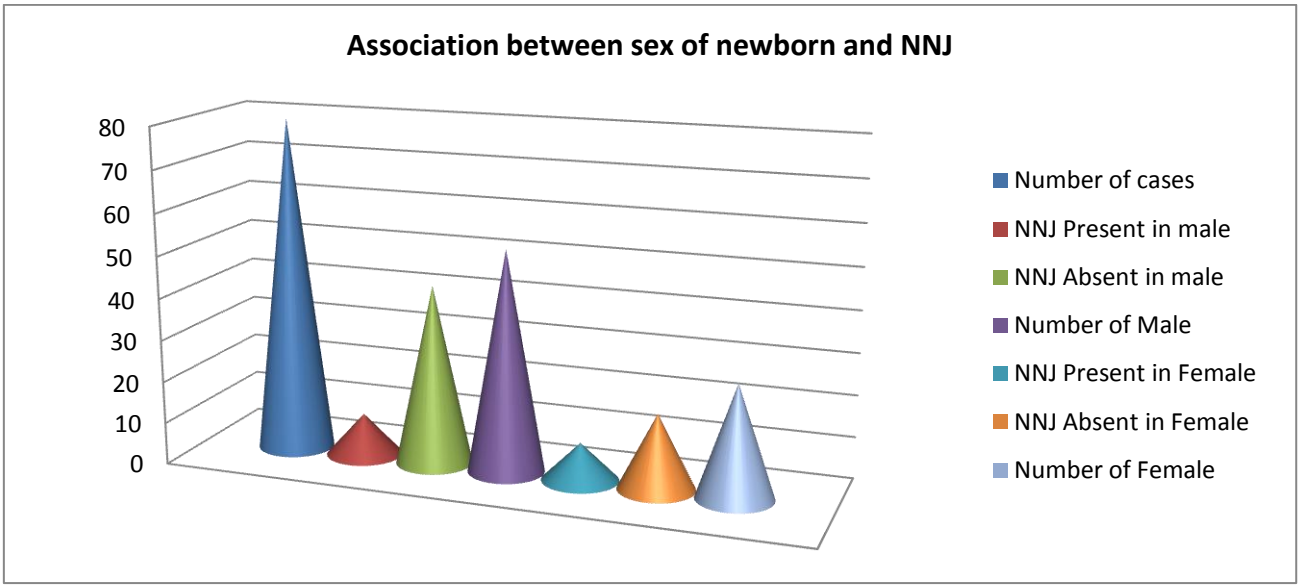
S.No	Types of Delivery	Numbers
1	Normal Vaginal delivery	49
2	Cesarean	31

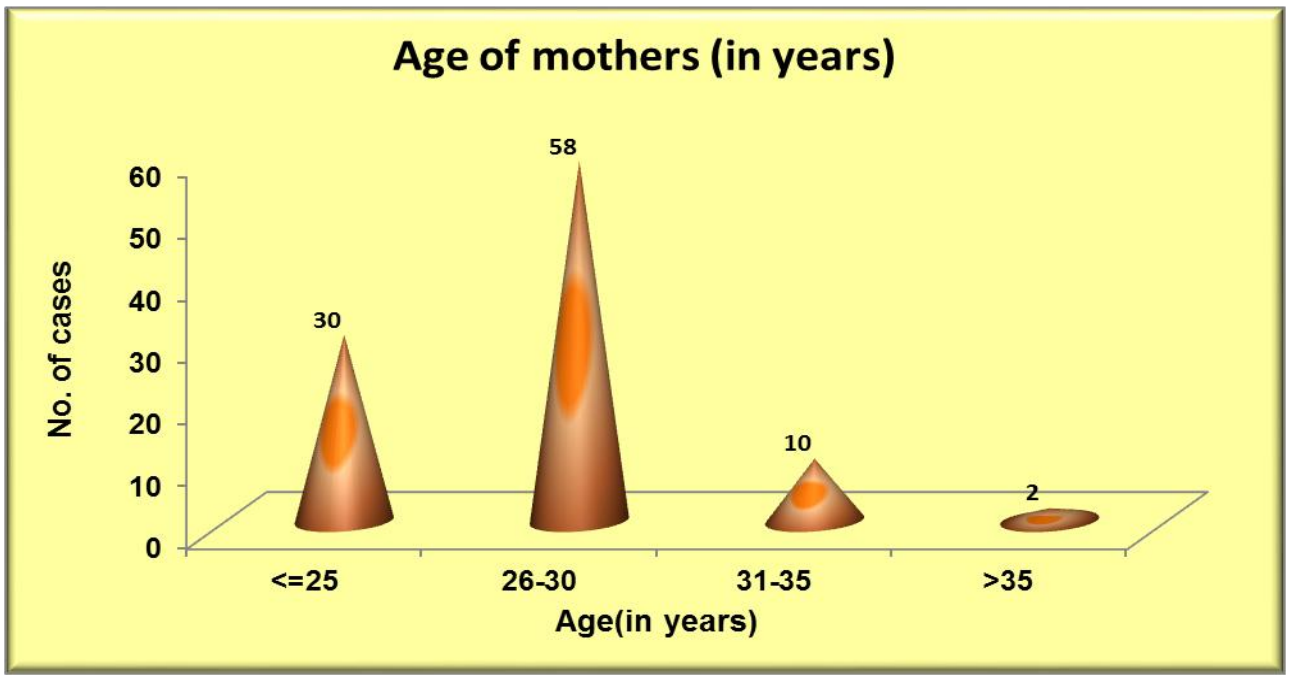
S.No	Types of Blood Groups	Numbers
1	A +ve	16 (20%)
2	B +ve	48 (60%)
3	AB +ve	12(15%)
4	0 +ve	4 (05%)

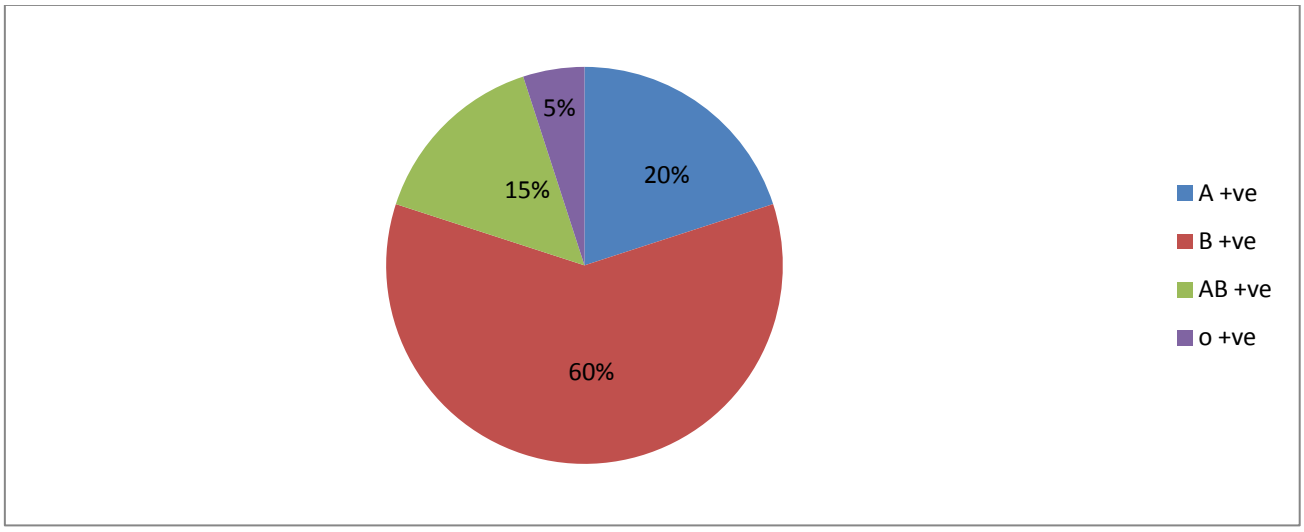
Study (No.of Cases)	UCS Bilirubin (mg/dl)	Incidence of Jaundice (%)
Present study (80)	0-0.9	0
	1 – 1.9	1.9
	2 – 2.9	14.5
	>3	80



Sex wise determination of Study Group







Association of NNJ and maternal blood group

DISCUSSION AND CONCLUSION

The study group consisted of 80 full-terms appropriate for gestational age neonates delivered in GMC, Haldwani (Uttarakhand) from July 2013 –Feb 2014. Incidence of hyper bilirubinemia was 14% in study population. Mean umbilical cord serum bilirubin was 1.63±0.73. There was no significant association between neonatal hyper bilirubinemia and route of delivery ($p>0.05$). No association was found between neonatal hyperbilirubinemia and sex of the baby and maternal age ($p>0.05$, not significant). The correlation between between the mother's blood group and the increased risk of hyperbilirubinemia in neonates was insignificant. Significant association was seen between neonatal hyper bilirubinemia and increasing umbilical cord serum bilirubin ($p= 0.001$).Using umbilical cord blood bilirubin level of ≥1.9 mg/dL hyperbilirubinemia could be predicted with sensitivity of 92.8% , specificity of 83.7% , positive predictive value of 48.1% and negative predictive value of 98.6%. Our data suggest that umbilical cord blood can be utilized for estimation of serum bilirubin to predict development of neonatal hyper bilirubinemia and decide need for appropriate intervention in healthy term neonates.

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