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Original Research Article

ETIOLOGICAL PROFILE OF NEONATAL HYPERBILIRUBINEMIA IN NEONATES IN NICU AT TERTIARY CARE CENTRE IN INDIA – A CROSS-SECTIONAL STUDY

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ABSTRACT

Background: Neonatal Hyperbilirubinemia is a one of the commonest clinical entities encountered in neonates in Neonatal Intensive Care Unit (NICU), if not identified early it can lead to significant morbidity and mortality. This study was carried out to find out the aetiology of neonatal hyperbilirubinemia in NICU. **Materials and Methods**: It was a single centre, cross-sectional, descriptive study of neonates having hyperbilirubinemia. The study was carried out in NICU of Department of Paediatrics in tertiary care centre over the period of 6 months from November 2024 to April 2025. The study population included neonates admitted in NICU having hyperbilirubinemia (Serum Bilirubin > 15mg/dl). The demographic data like name, sex, gestational age, age at onset of hyperbilirubinemia, birth weight was recorded. Data was collected based on laboratory investigations. **Results:** Total 81 neonates were included in the study. It was found that Male (61.73%) neonates had higher proportion of jaundice as compared to their female (38.27%) counterparts. Majority of hyperbilirubinemia was seen in full term (70.37%) neonates followed by Late Preterm and Preterms. It was observed that majority of neonates in the study had normal birth weight (72.84%) followed by LBW (27.16%). Physiological Jaundice was found to be as a predominant cause of hyperbilirubinemia followed by breastfeeding jaundice, Idiopathic, and Sepsis. All neonates in the study required phototherapy treatment to reduce the level of Jaundice and all neonates were discharged and there was no death during the study period. **Interpretation and Conclusion**: Hyperbilirubinemia is a common clinical problem in neonates in NICU and it is an important prognostic marker of various disease conditions in neonates. Thus, early identification and management of hyperbilirubinemia is essential to reduce the neonatal morbidity and mortality.

INTRODUCTION

Jaundice is a yellowish discoloration of the sclerae, skin and mucous membrane, due to deposition of bilirubin. When the total serum bilirubin is >15mg/dl, we call it as neonatal jaundice (hyperbilirubinemia).[1] Jaundice is most common in first week of life world-wide. It is seen in 60 % of full terms and 80% of preterms. It is more commonly seen in preterms than terms because of higher rates of bilirubin production due to shorter life span of red blood cells.[2] Jaundice is also most common cause for delayed discharge from hospital and readmission in NICU.[3,4]

Neonatal jaundice can be divided into physiological jaundice and pathological jaundice. Physiological jaundice occurs due to various different reasons. In neonates, there is increased enterohepatic circulation due to decreased intestinal motility which results in increased bilirubin resorption. Physiological volume restriction is also seen due to low volumes of breast milk. Delayed cord clamping is again a risk factor.[6] Bilirubin is a known antioxidant at low concentrations but a potent neurotoxin at high concentrations.[7] Free unconjugated bilirubin is neurotoxic and can damage neurons particularly in the basal ganglia and various brain stem nuclei, resulting in Acute Bilirubin Encephalopathy (ABE) manifested as lethargy, hypotonia, reduced Moro reflex and poor suckling.[8] Causes of pathological jaundice includes ABO incompatibility, Rh

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incompatibility, sepsis, G6PD deficiency and rarely autoimmune conditions.[9]

Etiology of neonatal jaundice may be unknown in significant number of cases. Although pathological jaundice has preference to be treated but threat of neurological damage is always high with high serum bilirubin levels and in presence of risk factors. In extreme cases, it can lead to acute bilirubin encephalopathy and ultimately to permanent and chronic neurological sequelae like cerebral palsy, deafness etc. these conditions are irreversible and so it becomes very important to prevent and diagnose early on. Identification of etiological factors and management leads to better prognosis.[3,4]

Phototherapy is safe and effective for treating uncomplicated pathological and physiological neonatal hyperbilirubinemia at home, according to a recent systematic study. Additionally, phototherapy at home can improve patient outcomes by reducing parental stress and anxiety, minimizing mother-infant separation, and encouraging breastfeeding and skin-to-skin contact.[10]

Fenofibrate was evaluated as an adjunct to phototherapy in newborns with Idiopathic hyperbilirubinemia in a number of RCTs. According to Khafaga et al., newborns with hyperbilirubinemia who received a single dose of fenofibrate (10 mg/kg) as an adjuvant to phototherapy saw a significant decrease in their serum bilirubin levels.[11]

The 2022 American Academy of Paediatrics guideline includes universal bilirubin screening, risk assessments for escalation-of-care (a new definition), updated nomograms for phototherapy and exchange transfusions with higher bilirubin thresholds than previous guidelines, and neurotoxicity risk factors that no longer include race as a risk factor.

When implementing the new guideline in low- and middle-income countries, care must be taken and local experts should be consulted because of the possible lack of resources for screening, treatment, and follow-up.

AAP 2022 defines 'neurotoxicity risk factor', which is a comparable but simplified concept. Hypoalbuminemia, haemolysis, and sepsis are also regarded as risk factors. Nevertheless, the new risk factor of "significant clinical instability within the past 24 hours" takes the place of the risk factors of asphyxia, significant lethargy, temperature instability, and acidosis in the updated guideline.[12]

Present study was undertaken to study the clinical profile and etiological factors leading to neonatal jaundice at our tertiary care centre.

MATERIALS AND METHODS

It was a single centre, Cross Sectional, descriptive study of neonates carried out in NICU of Department of Paediatrics in tertiary care centre. Study Population was neonates admitted in NICU having hyperbilirubinemia (Sr. Bilirubin > 15 mg/dl). While neonates whose parents refused to give consent, neonates having major congenital abnormalities and those who were born outside hospital having hyperbilirubinemia were excluded from the study. The sample size for this study was calculated with reference to statistical data,[13] using the following formula 4 pd/ d2. Neonates were enrolled in the study after obtaining written informed consent from parents/guardians. Study Period was 6 months from November 2024 to April 2025. Institutional ethical committee (IEC No - 4/2025) approval was obtained for the present study.

The demographic data like name, sex, gestational age, age at onset of hyperbilirubinemia, and birth weight was recorded. Information was obtained from parents/guardians of the recruited neonates on a range of demographic and clinical parameters.

The data collection instrument was a self-structured interviewer administered questionnaire that was pretested with modifications made prior to its use in the study.

Data was collected based on laboratory investigations. Sample was collected using Convenient Sampling Technique. The specimens of blood were collected on onset of day of jaundice. Blood Samples were obtained for the hyperbilirubinemia work up such as Liver Function Tests (Sr. Bilirubin, T/D, SGPT, SGOT), Sepsis work up, which included CBC (Complete Blood Count) and C-reactive protein (CRP) estimation. G6PD estimation, Blood group of the mother and baby, Coombs test were also done to find out the etiology of hyperbilirubinemia.

Statistical Analysis: Structured data-collecting forms were used to gather the data. Every observation and discovery were recorded into a Microsoft (MS) Excel (Microsoft® Corp., Redmond, WA) master spreadsheet, and then analyzed with the Epi Info software (Centers for Disease Control and Prevention, Atlanta, GA). Analysis was conducted using the Statistical Package for Social Sciences (SPSS) version 25 (IBM SPSS Statistics, Armonk, NY) and Epi Info version 7.3.

RESULTS

Table 1: Gestational age distribution among neonates

Gestational age	No. of Neonates	Percentage
Preterm (< 34 weeks)	04	04.94
Late-preterm (34 - 36+6 weeks)	20	24.69
Term (37 – 41+6 weeks)	57	70.37
Post-term (> 42 weeks)	00	00
Total	81	100

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The above table showed distribution of neonates according to their gestational age. It was observed that majority of neonates were term (70.37%) followed by late-preterm. (24.69%)

Table 2: Birth weight distribution among neonates

Birth weight (Kg)	No. of Neonates	Percentage
ELBW (<1)	00	00
VLBW (1-1.5)	00	00
LBW (1.5-2.5)	22	27.16
Normal (>2.5)	59	72.84
Total	81	100

The above table showed distribution of neonates according to birth weight. It was observed that majority of neonates had normal birth weight (>2.5 kg) (72.84%) followed by LBW (1.5-2.5 kg). (27.16%)

Table 3: Etiological distribution among neonates

Etiology	No. of Neonates	Percentage
Physiological jaundice	25	30.86
Breastfeeding jaundice	12	14.81
Idiopathic	11	13.58
Sepsis	09	11.11
ABO incompatibility	09	11.11
Rh incompatibility	06	07.41
G6PD deficiency	05	06.17
Breast milk jaundice	03	03.70
Polycythaemia	01	01.23
Total	81	100

The above table showed distribution of neonates according to etiology. It was observed that majority of neonates had Physiological Jaundice (30.86%) followed by breastfeeding jaundice (14.81%), Idiopathic (13.58%) and sepsis (11.11%).

Table 4: Mode of therapy distribution among neonates

Mode of therapy	No. of Neonates	Percentage
Phototherapy	81	100
Exchange transfusion	00	00
Total	81	100

The above table showed distribution of neonates according to mode of therapy. It was observed that total 100% neonates had phototherapy.

Table 5: Outcome distribution among neonates

Outcome	No. of Neonates	Percentage
Discharge	81	100
Death	00	00
Total	81	100

The above table showed distribution of neonates according to outcome. It was observed that total 100% neonates were discharged.

DISCUSSION

Neonatal jaundice is one of the most common causes of hospitalization of neonates in the first month after birth. In most cases, neonatal jaundice is transient and usually resolving at the end of the first week after birth. But when severe hyperbilirubinemia is present, there is a potential risk for acute bilirubin encephalopathy and kernicterus. This can lead to death in the first months, and infants who are still alive often suffer from mental retardation, movement and balance disorders, seizures, hearing loss at high frequencies, and speech impairment. So, timely diagnosis and treatment of neonatal jaundice are very important to prevent further complications.[14]

In this study, out of the total 81 neonates with jaundice, 50 (61.73%) were males and only 31(37.23%) were females. The results match the earlier studies done by Iqbal J et al, Babu et al and Korejo et al where majority of the babies were males.[15,16,17] Majority of the babies in our study were of term gestation 57 (70.37%) followed by late preterm 20 (24.69%) and then preterms 04 (4.94%). There was no post term baby in our study. A higher percentage of premature babies was found in studies done by Bhutani et al.[18] While a study done by Bashir U Zuman et al and Babu et al found the same results like in our study i.e majority of the babies they found jaundice were of term gestation while only < 20% were born of preterm gestation in both studies.[14,16] In our study, majority of the babies (72.84%) had normal birth weight. Only 27.16 % of the babies had birth weight less than 2500 gm. While we did not have any VLBW or ELBW baby in the study.

Similar results were seen in a study done by Nishad Patil et al where they found that 2500 - 4000 gm birthweight babies were 66 %, and 28% babies had birthweight less than 2500 gm.[19]

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While a study done by Ashish Kumar Pandey et al found that a significant proportion of neonates had a birth weight of less than 2500gms, representing 72.3% of the total, with the remaining 27.7% weighing 2500gms or more.[20]

As majority of the babies had normal birth weight in our study, we found that physiological jaundice as the major etiological factor i.e., 25 out of the total 81 babies (30%). This is in concordance to the study done by Bashir Uman et al and Babu et al wherein the physiological jaundice was observed in majority of the patients (40.5%) and (54%).[14,16] Studies done by Iqbal J et al and Mishra S et al observed physiological jaundice in 30.67% and 32% of the total cases respectively.[15,21] Breastfeeding jaundice as the second leading cause of neonatal jaundice in our study (14.81%). Similar results were seen in Nishad Patil et al where they found breastfeeding Jaundice in (12.65%) cases.[19] While in a study done by Bashir Uman et al found that breastfeeding jaundice was present in only 2% cases.[14] In our study, after breastfeeding jaundice, idiopathic variety was found to be responsible for 13.58% of the total cases. Similar results were seen by Nishad Patil et al where they found Idiopathic variety in (12%) neonates.[19] While in study done by Bashir Uman et al And Iqbal J et al found idiopathic variety only in 5% cases,[14,15] In our study, sepsis constituted 9% of the total cases studied. This is in concordance to earlier studies which showed a similar trend. Sepsis was found to be the cause of neonatal jaundice in 8% of neonates by Bashir Uman et al, 3.83% by Iqbal et al and 2% by Babu et al.[14,15,16] Contrary to our findings a high rate of sepsis (22.9%) was seen in a study done by Ashish Kumar Pandey et al.[20] This was followed by ABO incompatibility (11.11%) as the cause of neonatal jaundice in our study. This is in concordance to the studies done by Aga M et al and Pandey et al, wherein ABO incompatibility contributed to 19.1 and 18.8% of the cases.[9,20] After ABO incompatibility, Rh incompatibility was found to be responsible for (7.41%) of the total cases. Babu et al observed Rh incompatibility in 13% of the total cases while Patil et al reported an incidence of 4.12% for Rh incompatibility.[16,19] Thus, ABO incompatibility was more prevalent than Rh incompatibility. This is in concordance with older studies done abroad.[22,23] While a study done Syed et al found the equal incidence of ABO and Rh incompatibility (3.33%).[24] G6PD deficiency (6.1%), Breast milk jaundice (3.7%) and polycythemia (1.2%) were the remaining causes of hyperbilirubinemia found in the present study. All babies (81%) required phototherapy and none of them required exchange transfusion. In a study done by Choudhary Habibul Rasal et al Phototherapy was applied in most (62.6%) cases with good success and a small portion (5.2%) of patients underwent exchange transfusion.[25] In a study done by Aga M et al Intensive phototherapy was the most common form of treatment used for management of icterus in the study population; only 11 of 220 patients were required to undergo exchange transfusion.[9]

In our study, all babies were discharged and there was no death during the study period. In a study done by Choudhary Habibul Rasal et al,[12] (2.8%) patients in this study died in the hospital and 4 (0.9%) neonates were discharged with neurological sequelae.

CONCLUSION

This study concludes that physiological jaundice is the most common cause of neonatal jaundice in our hospital. This is followed by Breastfeeding Jaundice, Idiopathic, sepsis, ABO incompatibility, and Rh incompatibility. Hyperbilirubinemia is a common clinical problem in neonates in NICU and it is an important prognostic marker of various disease conditions in neonates. The study illustrates the multifactorial nature of neonatal jaundice and stresses the significance of prompt diagnosis, detection, and assessment of the underlying causes in addition to prompt intervention to tackle the condition. Thus, early identification and management of hyperbilirubinemia is essential to reduce the neonatal morbidity and mortality.

Limitations

There were some limitations to this study. As it was a single centre study the sample size was less. It is well known that there may be marked geographic variations in the pattern of etiological factors in neonatal jaundice. Therefore, our findings may not be reflective of the pattern in other regions. Another drawback was that some etiological factors leading to neonatal jaundice like Gilbert syndrome and Criggler-Najar syndrome were not investigated. Hence there is a possibility that some of the cases classified as idiopathic may have this underlying diagnosis.

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