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ORIGINAL RESEARCH

Clinico-Etiological Profile of Neonatal Hyperbilirubinemia in a Tertiary Care Hospital in North India

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ABSTRACT

Objective- To determine etiology of Neonatal Hyperbilirubinemia. To assess clinical features of Neonatal Hyperbilirubinemia and Hyper-bilirubinemic Encephalopathy (Kernicterus). To assess risk factors of Neonatal Hyperbilirubinemia. To correlate clinical severity of Hyperbilirubinemia with Transcutaneous Bilirubinometer (TcB) and Total Serum Bilirubin (TSB). **Methods**: - Hospital based cross-sectional observational study. The study was conducted in the NICU department of Pediatrics at Muzaffarnagar Medical College & Hospital, Muzaffarnagar, U.P. on indoor patients by following inclusion and exclusion criteria, conducting history taking, general physical examination, and relevant clinical examinations, according to predetermined questionnaire. **Results**: Firstly, concerning birth weight distribution, among the 96 neonates observed, a substantial proportion fell into the lower weight categories, with 47.9 % weighing less than 2500 grams, 29.2% falling within the 2500 to 2999 grams range, and the less, comprising 22.9 %, having a birth weight equal to or exceeding 3000 grams. This variation in birth weight underscores the diversity within the neonatal population. Secondly, the analysis of blood group incompatibility among neonates showed that 18.8% exhibited ABO incompatibility, 12.5% showed Rh incompatibility, while the majority (68.7%) displayed no blood group incompatibility. Thirdly, regarding neonatal jaundice onset time, the majority of cases occurred within the first week post-birth, with 10.4% within 24 hours, 37.5% on days 2-3, and 41.7% on days 4-7. This distribution highlights the critical need for monitoring neonates during this period to detect and manage jaundice promptly. Fourthly, the data on reticulocyte counts (%) in neonates revealed that 41.7% had counts of less than 2%, 37.5% fell within the 2-5% range, and 20.8% had counts exceeding 5%. **Conclusion:** These findings suggest varying degrees of erythropoietic activity during the neonatal period, which could have implications for overall health and development. The analysis of serum bilirubin levels and clinical severity indicated that 31.3% of neonates exhibited mild clinical severity, 46.9% showed moderate severity, and 21.8% presented severe severity.

Keywords: Hyperbilirubinemia, Pre-term, Term, Phototherapy, Neonatal Sepsis

INTRODUCTION

Hyperbilirubinemia often becomes an important clinical issue for newborns and requires much attention and treatment1. It has presented itself, historically, as a great public health challenge for two centuries now, in some areas such as South East Asia, tropical Africa, Pacific islands, and some Mediterranean countries; while often attributed to physiological factors, a small number of newborns develop jaundice levels in excess of the desired level that may culminate in severe brain damage.

Thus, bilirubin levels are below 1.0 mg/dl in normal adults whereas they are usually above this level in newborns. This rise in the level of bilirubin is due to one, shortened life span of red blood cells; two, increased bilirubin production due to hemolysis; three, immature enzyme systems in the neonate liver unable to deal with this load; four, increased activity of the beta-glucuronidase enzyme; five, inadequate bacterial colonization in the intestine; six, an increase in enterohepatic circulation due to the immature gastrointestinal tract of the neonates.

Approximately 85% of all full-term newborns and a vast majority of preterm newborns are reported to have developed clinical jaundice. Of the healthy full-term newborns, it is reported that 6.1%, on average, reach a peak serum bilirubin level greater than 12.9mg/dl, with 3% crossing the 15mg/dl.[1]

Moreover, hyperbilirubinemia is the leading cause for

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hospitalization of newborn. The trend of shortening hospital stays for mothers and newborns has increased over recent years due to various factors, which has facilitated earlier return to work for family members and lessened financial stress for families

The American Academy of Pediatrics defines early and very early discharge as occurring 48 and 24 hours after a smooth, normal vaginal birth, respectively, despite the fact that there is no universally accepted definition for either term[2].

Policies on early hospital discharge have led to an increase in readmissions of infants that can result from illnesses not apparent during the first two to three days of life[3]. Jaundice has emerged as one of the main reasons causing these readmissions [4-5]. In a 1995 study by Sola A et al., the re-emergence of bilirubin-induced encephalopathy and kernicterus was associated with early discharge from the hospital[6].

Kernicterus is a chronic and irreversible condition that results from bilirubin-bound in the brain in the first year of life, with clinical features of begun kernicterus often associated with a neonatal serum bilirubin concentration above 20 mg/dl.[7.8]. The risk may be alleviated with early, adequate phototherapy.

Risk factors for neonatal hyperbilirubinemia include cephalhematoma, significant bruising, sibling with a history of jaundice, immune-mediated hemolytic disease, gestational age of 35-36 weeks, and high or high-intermediate pre-discharge bilirubin level according to the Bhutani's nomogram. However much we understand, predicting accurately which newborns will develop jaundice remains difficult.

Hyperbilirubinemia is presented by the yellow pigmentation of the skin, sclera, and mucosa secondary to elevated bilirubin levels and is usually clinically evident when levels exceed 5 to 7 mg/dl. Jaundice occurs in all neonates, whether they are born term or preterm, and there is an increase in bilirubin in all.

METHODOLOGY

The study was conducted in the NICU department of Pediatrics at Muzaffarnagar Medical College & Hospital, Muzaffarnagar, U.P. on indoor patients by following inclusion and exclusion criteria, conducting history taking, general physical examination, and relevant clinical examinations, according to predetermined questionnaire. All neonates (>24 weeks gestation) with hyperbilirubinemia, neonates requiring phototherapy for the first time and neonates up to 28 days were included. While neonates planned for immediate exchange transfusion at the time of admission, neonates already started on phototherapy, >24 hours before referral, neonates <=24 weeks gestation, postnatal age beyond 28 days, small for gestational age (SGA)/IUGR, neonates with features of intrauterine infection, neonates with severe sepsis requiring ventilatory support, neonates having major congenital abnormalities, neonatal cholestasis and inborn errors of metabolism were excluded. Data were entered into a computerized database for statistical analysis. The mean, standard deviation, standard error of mean, standard error of difference, t- value, and 95% confidence intervals of various variables were calculated. The statistical significance of the difference in the rate of an outcome between the two groups was assessed by a χ 2-test. CBC, TSB, Peripheral smears, CRP levels, Blood group and other relevant investigations were assessed.

RESULTS

The findings from our study reveal significant insights into various aspects of neonatal health. Firstly, concerning birth weight distribution, among the 96 neonates observed, a substantial proportion fell into the lower weight categories, with 47.9 % weighing less than 2500 grams, 29.2% falling within the 2500 to 2999 grams range, and the less, comprising 22.9 %, having a birth weight equal to or exceeding 3000 grams. This variation in birth weight underscores the diversity within the neonatal population. Secondly, the analysis of blood group incompatibility among neonates showed that 18.8% exhibited ABO incompatibility, 12.5% showed Rh incompatibility, while the majority (68.7%) displayed no blood group incompatibility. These findings emphasize the importance of screening and monitoring neonates for blood group compatibility to prevent potential complications. Thirdly, regarding neonatal jaundice onset time, the majority of cases occurred within the first week post-birth, with 10.4% within 24 hours, 37.5% on days 2-3, and 41.7% on days 4-7. This distribution highlights the critical need for monitoring neonates during this period to detect and manage jaundice promptly. At the same time, neonatal reticulocyte counts (%) proved that 41.7% fell below 2%, 37.5% were within 2-5%, and 20.8% were greater than 5%. The findings indicate various levels of erythropoietic activity, which may affect their overall health and development. 31.3% of neonates had mild severity, 46.9% had moderate severity, and severe ranged up to 21.8% of neonates as assessed by clinical severity matched with serum bilirubin levels.

The Figure: 1 displays data pertaining to 96 babies with neonatal factors and the percentage of their prevalence. These included: 18.8% prematurity, 20.8% feeding difficulties, 22.9% sepsis, and 10.4% birth trauma. Importantly, of the babies, 27.1% presented with no identified factors associating with their condition. This data speaks to the multi-factorial nature of neonatal pathology.

Health challenges, emphasizing the importance of comprehensive care and targeted interventions to address diverse issues in neonatal healthcare.

The Figure: 2 presents the etiology of neonatal jaundice, with a total of 96 cases were analyzed. Among the identified causes, hemolytic causes accounted for the highest proportion at 36.4 %, followed by sepsis at 28.1 %, notably, a significant portion, comprising 35.4 %, fell under the category of

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idiopathic, indicating cases where the specific cause of jaundice remained unidentified. This breakdown underscores the diverse factors contributing to neonatal jaundice, with hemolytic causes emerging as the most prevalent known cause in the studied population.

Figure: 3 presents the distribution of neonates based on their bilirubin levels and corresponding clinical severity. Among the 96 neonates assessed, 31.3% exhibited mild clinical severity with bilirubin levels below 10 mg/dL, 46.9% showed moderate severity with levels between 10- 15 mg/dL, and 21.8% presented severe clinical severity with bilirubin levels exceeding 15 mg/dL. This data underscores the prevalence of neonatal jaundice and highlights the varying degrees of severity necessitating clinical attention and management.

The figure: 4 depicts the correlation coefficients between Total Serum Bilirubin (TSB), Transcutaneous Bilirubin (TcB), Gestational Age, Birth Weight, and Reticulocyte Count. The count of total serum bilirubin and transcutaneous bilirubin showed a powerful positive correlation of 0.9, indicating a strong relationship between these two measures of bilirubin levels. Gestational Age shows a moderate correlation with both TSB (0.5) and TcB (0.4), suggesting that higher levels of bilirubin tend to accompany a progress in gestational age. Likewise, birth weight shows a moderate positive correlation with TSB (0.5) and TcB (0.4), indicating that higher birth weights may be associated with higher bilirubin levels. Meanwhile, reticulocyte count shows a weak positive correlation with TSB (0.5) and TcB (0.4), suggesting that there may be some relationship between reticulocyte count and it might influence serum bilirubin count. Overall, the table offered insight about how these variables could interact in the assessment of bilirubin levels. Both of the measures, total serum bilirubin and transcutaneous bilirubin, showed a very strong positive correlation with a coefficient of 0.9, thus reflecting a much stronger correlation between these two measures of bilirubin levels. Moreover, gestational age is moderately correlated with total serum bilirubin (0.5) and transcutaneous bilirubin (0.4), which would mean bilirubin increase with gestational age. Similarly, the birth weight also has a moderate positive correlation with total serum bilirubin (0.5) and transcutaneous bilirubin (0.4), revealing that larger birth weights may be linked to higher bilirubin. The reticulocyte count shows a weaker positive correlation with total serum bilirubin and transcutaneous bilirubin, suggesting that a weaker relationship may exist between reticulocyte count and serum bilirubin levels. The table gives an account of how the interplay among these variables may affect the assessment of bilirubin levels.

Total Serum Bilirubin (TSB) and Transcutaneous Bilirubin (TcB) are highly positively correlated (r = 0.9), which makes sense as they both measure bilirubin levels, albeit through different methods.

Gestational Age and Birth Weight are positively correlated (r = 0.7), indicating that babies born at a later gestational age tend to have higher birth weights. Total Serum Bilirubin (TSB) shows a negative correlation with Gestational Age (r = -0.4) and Birth Weight (r = -0.3), suggesting that lower gestational age and birth weight are associated with higher bilirubin levels.

Reticulocyte Count has a moderate positive correlation with Total Serum Bilirubin (TSB) (r = 0.5), indicating that increased reticulocyte count, which may suggest hemolysis, is associated with higher bilirubin levels.

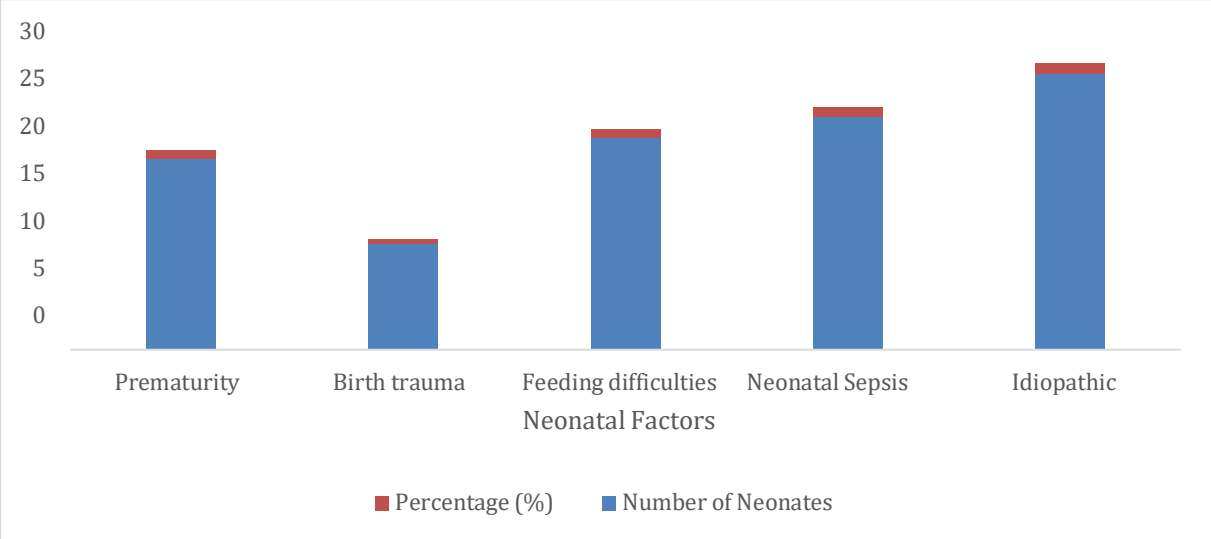

Fig 1: Incidence of Hyperbilirubinemia in Relation to Neonatal Factors

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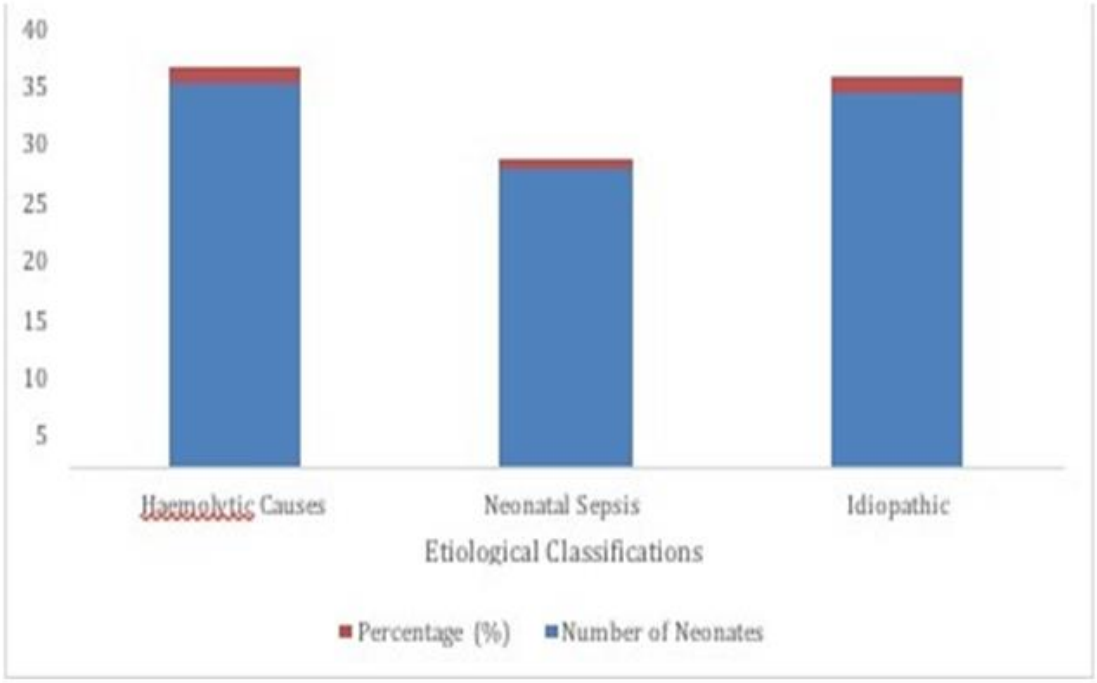

Fig 2: Etiological Classification of Hyperbilirubinemia

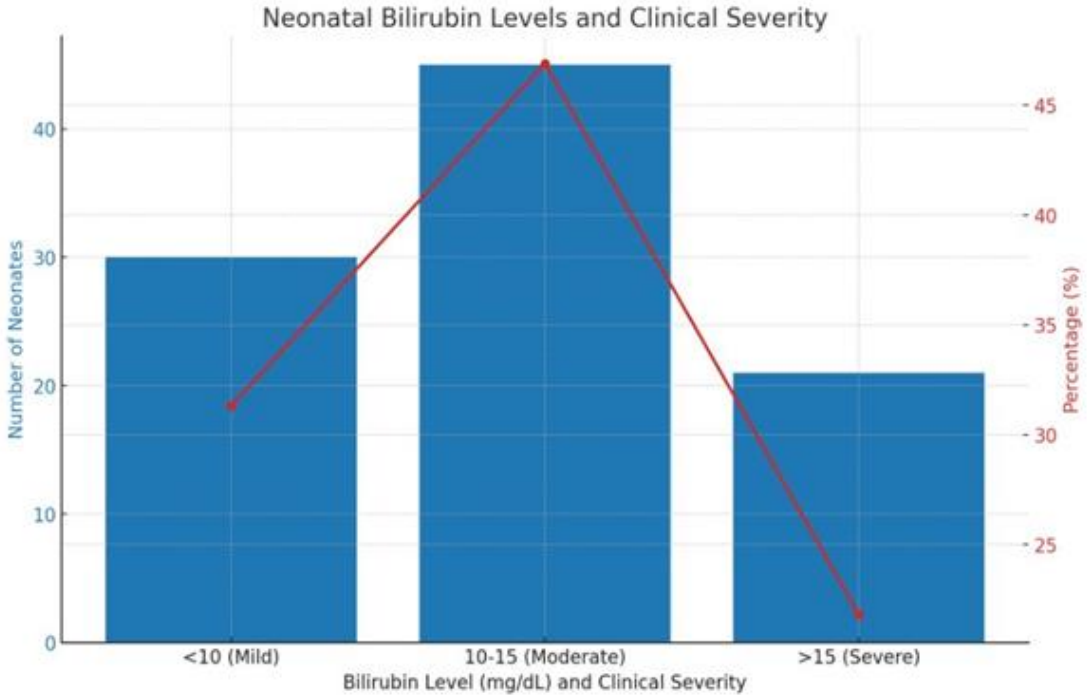

Fig 3: Serum Bilirubin Levels and Clinical Severity

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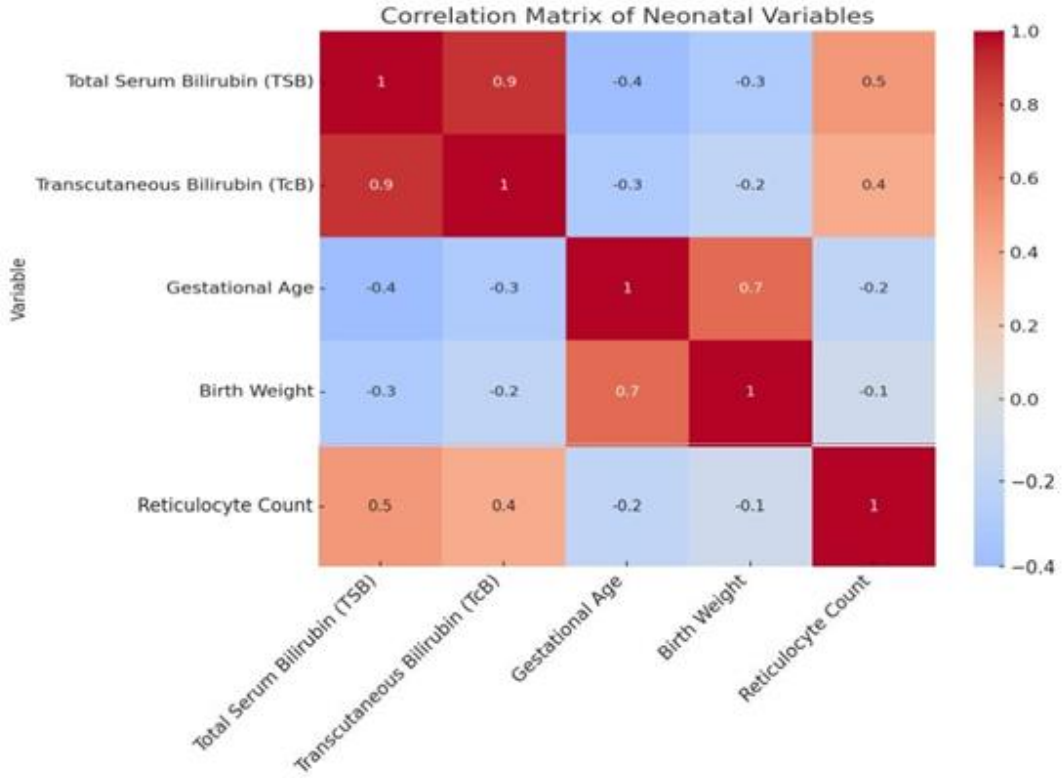

Fig 4: Correlation Coefficients among Clinical and Laboratory Variables in Neonatal-Hyperbilirubinemia

DISCUSSION

The study provides valuable insights into the demographics of neonates, shedding light on their age distribution, gender representation, and gestational age. In terms of age distribution, the majority of neonates (37.5%) were within the five-day age range, followed by 2-4 days (31.3%), 1st day (20.8%), and 8-14 days (10.4%). This indicates a concentration of neonates within the first five days of birth. Moving to gender distribution, the study shows a balanced representation between males (52.1%) and females (47.9%) among the 96 neonates surveyed. This equal split suggests no significant gender bias in the population studied. Regarding gestational age distribution, it's observed that 45.8 % of neonates were born preterm (<37 weeks), 35.8 % at term (37-41 weeks), and 18.8 % post-term (≥ 42 weeks). Notably, a substantial proportion of neonates were born at pre-term, with a notable presence of term births. These findings contribute to our understanding of neonatal demographics within the studied population, facilitating targeted interventions and healthcare planning to meet the specific needs of different neonatal groups.

Jena D et al., investigated the demographic profile of neonates, focusing on both inborn and out born cases. They found that the average age at admission for out born neonates was 5.42 days, with a standard deviation of 2.58 days, while for inborn neonates, it was slightly lower at 3.96 days, with a standard deviation of 3.03 days. Looking at the age distribution, the majority of neonates admitted were within the 0-7 days age range with average age at admission was 4.52 days, with a standard deviation of 2.73 days constituting 67.7% of out born and 32.3% of inborn cases. Furthermore, regarding gender, they observed a predominance of males, comprising 63.9% of the total neonates studied, with females accounting for the remaining 36.1%. In terms of gestational age, most neonates were born at term, making up 89.6% of the total, while pre-term births constituted 10.4%. Similarly, 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. Overall, our findings highlight the diverse demographic characteristics of neonates admitted to our study, shedding light on important factors that may influence their health outcomes.

Our study delved into the severity and etiology of neonatal jaundice, shedding light on its multifaceted nature. In analyzing the severity of cases, we found a distribution across mild, moderate, and severe categories. Among 96 neonates observed, 31.3% exhibited mild symptoms, 46.9% displayed moderate symptoms, and 21.8% faced severe manifestations. This breakdown underscores the varying degrees of impact the condition can have on newborns. Our investigation into the underlying causes revealed a diverse landscape. Hemolytic causes emerged as the

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most prevalent etiology, contributing to 36.4% of cases. Following closely behind was neonatal sepsis, accounting for 28.1%. Intriguingly, a considerable proportion, 35.4%, remained idiopathic, indicating cases where the specific cause of jaundice eluded identification. This comprehensive breakdown highlights the intricate interplay of factors contributing to neonatal jaundice, with hemolytic causes standing out as a prominent known contributor. Alizadeh Taheri P et al., investigating the underlying causes of severe hyperbilirubinemia leading to exchange transfusion (ET), they analyzed the onset of jaundice and associated predisposing factors. Among newborn exhibiting jaundice on the first day after birth, ABO mismatch was the most common cause, accounting for 7.4%, followed by Rh mismatch (2.1%). On the second day, ABO mismatch remained prominent (13.82%), along with breast feeding jaundice (9.6%) and sepsis (8.5%). By the third day, breast feeding jaundice became the most prevalent cause (14.9%), alongside sepsis (3.2%) and ABO mismatch (3.2%). On subsequent days, Rh mismatch, and breast-feeding jaundice continued to contribute to severe hyperbilirubinemia. Regarding predisposing factors, hemolytic conditions accounted for 24.5% of cases, with ABO mismatch, Rh mismatch, being significant contributors. Non-hemolytic factors were more common, with breast feeding jaundice and prematurity prevailing. These findings underscore the multifactorial nature of severe hyperbilirubinemia, emphasizing the importance of early identification and intervention to prevent complications like ET45.

Our study delved into the clinical manifestations of Kernicterus in neonates, revealing intriguing insights into the spectrum of symptoms observed. High-pitched cry emerged as the most prevalent manifestation, affecting 8.33 % of the neonates studied, highlighting its prominence as a sign of the condition. Following closely behind, poor feeding was noted in 4.16 % of cases, indicating its substantial impact on affected newborn. Additionally, lethargy was documented in 3.12 % of neonates, shedding light on its association with Kernicterus. Notably, hypertonia and seizures were reported in 2.08 % and 1.04 % of cases, respectively, underlining the neurological implications of the condition.

CONCLUSION

The in-depth study on neonatal hyperbilirubinemia from a tertiary care hospital in North India is an informative study into the clinical and etiological profiles, risk factors, and outcome of this common neonatal condition. The study conveys that neonatal jaundice is multifactorial and emphasizes the importance of timely detection, diagnosis and evaluation of causes coupled with intervention well on time to tackle the problem. The study elucidates the very fact that neonatal jaundice is multifactorial, signifying the key role played by early diagnosis, etiological assessment, and timely intervention in the effective management of this condition.

Neonatal hyperbilirubinemia presents itself as a prominent problem, with many babies showing up with the condition soon after birth. The investigation points towards hemolytic reasons and infections as the main causes, whereas idiopathic causes constitute a remarkable fraction. This diversified etiology necessitates a meticulous clinical and laboratory assessment to unmask the etiological factors involved. Risk factors include blood group incompatibility, maternal diabetes, and preterm. This emphasizes the need for antenatal and perinatal care in the management of hyperbilirubinemia. Furthermore, it highlights the effectiveness of phototherapy and other therapies in saving most affected infants, although a small proportion of neonates failed to respond to treatment. This indicates that alternate or adjunct therapy needs consideration in such situations.

That is why the clinical severity in connection with laboratory findings, especially total serum bilirubin versus transcutaneous bilirubin levels, serves as the basis for non-invasive screening and monitoring strategies. Additionally, the combined influence of maternal and neonatal factors could also be an indicator of the incidence and severity of hyperbilirubinemia; hence, the understanding of the condition is complex and requires multidisciplinary care.

In conclusion, this study increases the understanding of neonatal hyperbilirubinemia early, proper evaluation, and timely intervention to avoid complications and ensure good outcomes among neonates. The results suggest a need to carry out further research, especially with the idea of idiopathic causes of this concern as well as new modalities for therapy to achieve improved care for affected neonates.

ETHICAL APPROVAL

The study was approved by the Institutional Ethics committee.

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