

A study of neonatal hyperbilirubinemia from a tertiary care hospital in Northern India

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ABSTRACT

Objective: The objective of this study was to analyze the incidence of pathological jaundice, average time of presentation, mean duration of phototherapy, and need for exchange transfusion with appropriate medical management. **Methods:** Thus, retrospective study was conducted at neonatal intensive care unit of a tertiary care hospital from August 2017 to August 2018. All live births who were diagnosed with neonatal hyperbilirubinemia and requiring treatment were included in the study. Exclusion criteria included any baby with conjugated serum bilirubin >20% of total serum bilirubin or >2 mg/dl or neonate with any congenital malformation. **Results:** Nearly 5% of total babies delivered developed neonatal jaundice requiring treatment. The most common causes isolated were ABO incompatibility followed by Rh incompatibility. Almost 46% of babies were not found to have any cause. The most likely etiology concluded in this group was breastfeeding jaundice. **Conclusion:** Breastfeeding jaundice should be considered as one of the common causes of pathological jaundice making lactational counseling during antenatal and postnatal period an essential component of management and prevention of pathological jaundice. Early detection and timely intervention with lesser invasive treatment modalities such as intravenous immunoglobulin G, hydration, and phototherapy should be attempted aggressively to avoid need for high-risk procedures like exchange transfusion.

Key words: Bilirubin, Immunoglobulin, Jaundice, Neonate, Phototherapy

Neonatal jaundice is noted in >50% of newborns [1,2]. It is more often physiological; however, sometimes serum bilirubin levels cross the normal range (as per the recommended guidelines by the American Academy of Paediatrics [AAP] [$<1-2$ mg/dl/4 h] [3]) to become pathological [3,4]. If timely detected and treated appropriately for underlying cause, severe consequences like bilirubin encephalopathy can be prevented. Severe hyperbilirubinemia warrants need for exchange transfusion which itself carries lot of complications. Hence, it is essential to understand about the science of neonatal jaundice, underlying causes and interventions, so as to decrease the need for exchange transfusion. We conducted this study to analyze the incidence of pathological jaundice, average time of presentation, possible causes of jaundice, mean duration of phototherapy, medical management, and need for exchange transfusion.

MATERIALS AND METHODS

This was a retrospective study conducted in a tertiary care hospital which included all live births who were diagnosed with neonatal hyperbilirubinemia requiring treatment from August 2017 to August 2018. Exclusion criteria included any baby with conjugated serum bilirubin >20% of total serum bilirubin or >2 mg/dl or neonate with any congenital malformation.

A detailed history was recorded from patient's files; details such as physical examination and blood reports were noted. Serum bilirubin was measured by Jendrassik and Grof method by fully automated analyzer. Data were also recorded at the time since birth for the appearance of pathological jaundice, duration of phototherapy, need for exchange transfusion, intravenous immunoglobulin, and intravenous fluid requirement.

As a protocol in our neonatal intensive care unit (NICU), all babies with neonatal jaundice requiring phototherapy were given maintenance fluids and 40% of maintenance fluids as extra to compensate for warmer and phototherapy losses. Maintenance fluids were given in the form of feeds in all babies who tolerated orally and the babies with neonatal hyperbilirubinemia were started on double surface phototherapy. All phototherapy units are of same quality and adjusted similarly for distance and wavelength (Lullaby [GE], Zeal medical; 420–470 nm wavelength).

Statistical analysis was performed in Microsoft Excel sheet using descriptive statistics, whereby mean and standard deviations were calculated for the required data.

RESULTS

The total number of live births delivered over a duration of 13 months was 2535 (610 lower segment cesarean section

[LSCS] and 1925 NVD), of which 128 babies were treated for neonatal hyperbilirubinemia. Of 128 babies, 63 were female and 65 males. Among 128 neonates, 3.9% were extremely low birth weight (LBW), 9.3% very LBW, 14% LBW, and 72.6% normal birth weight and the mean birth weight was 2.93 ± 0.47 kg. Nearly 33% (42/128) of babies were delivered to primigravida mothers. Of 128 babies, 43 (33.5%) were delivered by LSCS and rest 85 babies (66.4%) by vaginal route. The mean age at presentation in NICU for the treatment of neonatal jaundice was 61.5 ± 31.3 h. Mean serum bilirubin at the time of starting phototherapy was 16.8 ± 3.36 mg/dl. On evaluating the causes of neonatal hyperbilirubinemia, we recorded that 26.5% (34/128) of babies had ABO incompatibility, 12.5% (16/128) were Rh incompatible, 7.8% (10/128) babies showed clinical or laboratory evidence of sepsis, 2.3% (3/128) had cephalhematoma, and 4.6% (6/128) had polycythemia. No cause was found in rest 46% (59/128) of neonates (Fig. 1). Direct Coombs test was positive in four children, three being Rh incompatible and one ABO incompatible and the reticulocyte count ($>3\%$) was increased in 21 children. Of these, all babies who were neither Rh nor ABO incompatible were checked for deficiency of glucose-6-phosphate dehydrogenase (G6PD), and none of the babies were found to be G6PD deficient. Of 128 babies, 120 accepted oral feeds as maintenance fluids, rest eight babies were given maintenance fluids intravenously. All babies were given extra 40% of maintenance fluids by intravenous route. Normal saline bolus of 20 ml/kg was given in nine babies who showed the evidence of dehydration, lethargy, poor feeding, decreased urine output, or increased capillary refilling time. Babies who had non-hemolytic jaundice falling near exchange range or the fall in serum bilirubin was less than the recommended guidelines by AAP, breastfeeds were replaced by formula feeds.

The mean duration of phototherapy was 32.19 ± 20.9 h. Intravenous immunoglobulin was given in six children (three Rh incompatible, two ABO incompatible, and one sepsis) at 2 g/kg over 2 days. Partial exchange with normal saline was done for four babies, all having a hematocrit $> 65\%$ and serum bilirubin

crossing the phototherapy range. None of the babies required double volume or single volume exchange transfusion. One baby (Rh incompatible and DCT positive) required packed cell transfusion.

DISCUSSION

Our study showed that nearly 5% of newborn babies developed neonatal hyperbilirubinemia requiring treatment. The incidence was comparable in males and females. We noted that the most common etiology isolated as the cause of jaundice was ABO incompatibility noted in 27% of babies. An Indian study done by Shetty and Kumar [2] also concluded ABO incompatibility as the most common cause in 13.47% cases. Similar results were shown by Davutoglu M *et al.* from Turkey [5].

An important finding noted in our study was that nearly 46% of babies were not found to have any cause of neonatal hyperbilirubinemia. The study by Shetty and Kumar conducted in Southern India was also unable to find a cause in one-third of the cases, very similar to our study. After reviewing literature and previous studies, we found that the most likely causes for this group with yet unknown etiology are breastfeeding jaundice and genetic variability.

Breastfeeding jaundice develops in 13% of exclusively breastfed infants during the 1st week of life. Inadequate breastfeeding adds to dehydration which significantly contributes to increase in serum bilirubin levels. A study by Xavier *et al.* [1] showed that inadequate breastfeeding contributes to 50% of non-physiological jaundice. According to same, aggressive lactation support with daily weight monitoring can reduce the requirement of phototherapy by 30%. The increase in serum bilirubin in inadequately breastfed babies is similar to increase in serum bilirubin seen with partial starvation in adults [6,7]. Another study has shown 5-fold increase in intestinal bilirubin absorption in newborn rhesus monkeys in spite of normal feeding [8]. Poor feeding leads to delay in emptying of meconium further adding to increased serum bilirubin levels [9]. Adequacy of breastfeeding can be assessed by multiple parameters [10]. An objective measurement is weight monitoring where body weight loss $>7-10\%$ in term babies by day 3 is considered as inadequate feeding [11]. In our study also, the mean weight at start of treatment was 10.3% less than the birth weight at mean age of 61 h, suggesting inadequate feeding. Unfortunately, a lot of mothers have been found to be facing feeding problems and require repeated lactation counseling, but the non-availability of counselors has added to inadequate breastfeeds in babies. Due to shortage of resources, daily weight monitoring could not be checked in babies admitted in postnatal wards. Our average time for presentation was 60 h which coincided with the time of appearance of breastfeeding jaundice. Considering breastfeeding jaundice as one of the most important causes in our settings, we gave 40% extra fluids for warmer and phototherapy losses. This extra fluid was meant to overcome any underlying dehydration and increased renal excretion of bilirubin. In patients with obvious features of dehydration, normal saline bolus was given. We further

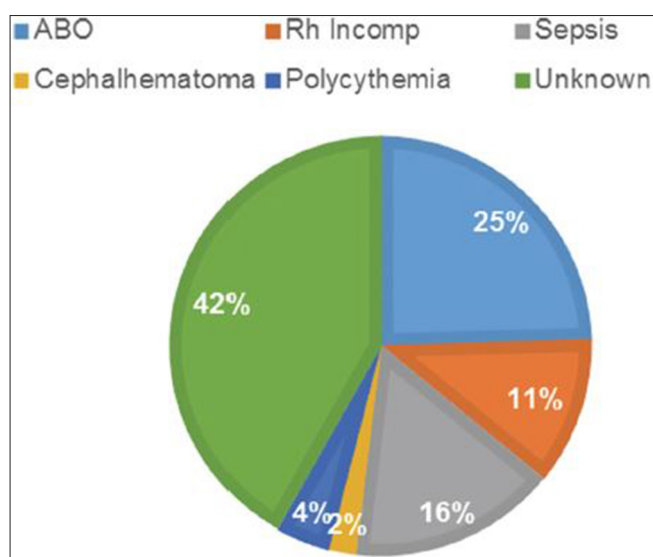


Figure 1: Percentage distribution of the causes of jaundice

noted that using this regime our babies responded very well to phototherapy with none of them requiring exchange transfusion. Fluid supplementation in severe hyperbilirubinemia has been well studied in literature. A study by Bandyopadhyay and Maiti [12] had shown that fluid supplementation along with DSPT in term neonates with severe hyperbilirubinemia significantly decreases the rate of exchange transfusion and duration of phototherapy. Another study by Goyal *et al.*, in 2018 [13], has shown that 50 ml/kg intravenous fluid supplementation results in faster decline of STB in first few hours of treatment.

Our mean duration of phototherapy was 32 h with cochlear implants ranging from 11 h to 53 h. This duration includes even those babies who had underlying hemolysis or sepsis as the cause of jaundice, further suggesting that breastfeeding jaundice may be contributing to increase in serum bilirubin levels in such babies. An added genetic cause for jaundice is yet another possibility in babies with no obvious cause and needs further research. Some such conditions like Gilbert syndrome need further evaluation to ascertain their incidence.

An important outcome noted in our study was avoidance of exchange transfusion by timely use of intravenous immunoglobulin G (IVIG) where six babies required IVIG. These babies either had a very high serum bilirubin or the fall in serum bilirubin on phototherapy was less than the recommended guidelines by AAP [14,15]. Further, evaluation showed that all six babies had an underlying cause as discussed previously. None of the babies showed any signs of bilirubin encephalopathy at any time of admission. Understanding the cumbersome process of exchange transfusion and the associated risks of adverse events [16], a less invasive strategy to decrease the rate of exchange transfusion should be considered. We further tried to limit the increase in serum bilirubin due to breakdown of excess red blood cells in babies with increased hematocrit in spite of hydration by partial exchange with normal saline. This is comparatively a safer procedure with less adverse effects when compared to exchange transfusion.

Our 1-month follow-up of 92 babies showed no clinical signs of neurological deficit. BERA and retinopathy of prematurity screening were done in babies who required IVIG/exchange transfusion and were found to be within normal range.

CONCLUSION

Breastfeeding jaundice should be considered as one of the common causes of pathological jaundice making lactational counseling during antenatal and postnatal period an essential component of management and prevention of pathological jaundice. Early

detection and timely intervention with lesser invasive treatment modalities such as IVIG, hydration, and phototherapy should be attempted aggressively to avoid need for high-risk procedures like exchange transfusion.

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