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Original Research Article

Clinico-etiological profile of neonates with neonatal hyperbilirubinmemia treated with double volume exchange transfusion

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ABSTRACT

Background: Neonatal hyperbilirubinemia continues to be the most common cause of hospital admissions and readmissions in the neonatal population worldwide and this pattern continues despite attempts to identify neonates at risk of pathological hyperbilirubinemia. The aim of the study was to determine the clinical profile and etiology in neonates who were treated with double volume exchange transfusion (DVET).
Methods: This was a hospital based prospective observational study in neonates ≥35 weeks of gestation who were treated with DVET for severe hyperbilirubinemia in a tertiary care centre over a period of six months.
Results: In our study 110 neonates with severe hyperbilirubinemia were treated with DVET. Majority of the neonates were males (59.1%). Lower segment caesarean section (LSCS) was the common mode of delivery observed in 66.4% of the study subjects. Rh incompatibility (36.4%) was the commonest cause of exchange transfusion followed by ABO incompatibility (20%). The mean age of neonates at admission and mean age at DVET in days were 4.03±2.46 and 4.25±2.44 respectively. The mean birth weight of neonates treated with DVET was found to be 2.81±0.57. The mean total serum bilirubin at pre-exchange and post exchange were 26.13±6.58 mg/dl and 11.63±3.24 mg/dl respectively.
Conclusions: Rh incompatibility was the most common cause in neonates with severe hyperbilirubinemia requiring double volume exchange transfusion.

Keywords: Double volume exchange transfusion, Neonatal hyperbilirubinemia, Rh incompatibility

INTRODUCTION

Neonatal hyperbilirubinemia is a common cause of admission to the neonatal intensive care unit (NICU).[1] About 50% of term and 80% of preterm babies develop jaundice during the neonatal period but only 0.02-0.16% develop extreme hyperbilirubinaemia.[2,3] Breast milk jaundice, ABO incompatibility, Rh incompatibility, Glucose-6-phosphate deficiency (G-6-PD), East Asian ethnicity and cephalhaematoma are conditions associated with severe jaundice.[4] The serum bilirubin level varies with birth weight, gestational age, chronological age and internal milieu of the body. When total serum bilirubin level exceeds a critical limit, it crosses the blood brain barrier and results in bilirubin encephalopathy.[5] Kernicterus and BIND are often used interchangeably although Kernicterus is a pathological diagnosis and BIND as clinical diagnosis.[6] Kernicterus is a preventable condition. Although BIND are rare in high income countries, it is still more common in low income country.[7] Exchange transfusion (ET) is considered to be the most effective and quickest method to lower the bilirubin level in infants at high risk of BIND.[8] But there is risk of complication related to procedure and metabolic and hematological alteration.[9] Recently, the number of ETs has been significantly reduced due to the availability of highly effective double surface and LED phototherapy and intravenous immunoglobulin G (IVIg) in prevention of isoimmunization/blood group incompatibility.[10] ET is sufficient to minimize brain damage, despite the adverse

event.[11] The aim of the study was to determine the clinical profile and etiology in neonates who were treated with double volume exchange transfusion (DVET).

METHODS

This was a hospital-based prospective observational study conducted in the neonatology unit of Department of Pediatrics, Government Medical College Srinagar, Jammu and Kashmir after approval from the institutional ethical committee. The study was conducted over a period of six months from August 2023 to January 2024.

Written informed consent was obtained from all the parents/guardians of the enrolled subjects. All neonates presenting with neonatal hyperbilirubinemia with gestation ≥35 weeks with hyperbilirubinemia in exchange range according to the American Academy of Pediatrics (AAP) guidelines were included in the present study. Neonates of less than 35 weeks' gestation, Apgar score <5 at 5 min, any stage of hypoxic ischemic encephalopathy, major congenital malformations, conjugated hyperbilirubinemia, metabolic disorders and DVET other than the cause of neonatal hyperbilirubinemia were excluded from the study.

Maternal demography and neonatal characteristic data were collected. Neonatal age, sex, birth weight, blood grouping and Rh typing, age on admission, treatment history at referral hospital and maximum bilirubin, age on exchange transfusion, type of feeding, sibling requiring phototherapy and exchange transfusion, physical examination, gestational age, admission weight, dehydration and weight loss, presence of acute bilirubin encephalopathy, cephalohematoma, total serum bilirubin (TSBR) at admission were collected. Investigations such as blood glucose, total, direct and indirect serum bilirubin (SB), ionized calcium, haematocrit, haemoglobin, total and differential leucocyte counts, platelet counts and peripheral blood smear, reticulocyte count and direct Coombs test were performed.

ABO and Rh blood grouping of both baby and mother were done. Neonates who were suspected to have sepsis were investigated by complete blood count, septic screen and blood and urine cultures. Neonates were managed according to the American Academy of Pediatrics, 2004 guidelines. Double volume exchange (160 ml/kg) transfusion (DVET) was performed with push pull technique from the umbilical vein or by peripheral artery using fresh whole blood within 5 days of collection.

Statistical analysis

Results were described using measures of central tendency, mean and standard deviation for continuous data with a normal distribution or median and range for skewed data. Categorical variables were described as frequency and percentage.

RESULTS

Out of the total 110 neonates requiring exchange transfusion, who fulfilled the inclusion criteria, 65 (59.1%) were males and 45 (40.9%) were females. 73 (66.4%) neonates were delivered via LSCS and 37 (33.6%) were delivered via NVD. In this study, majority of the babies (n=84, 76.4%) were born at term and the rest (n=26, 23.6%) were born pre-term. Out of the total 110 study subjects, 83 (75.5%) had birth weight ≥2500 grams and 27 (24.5%) had birth weight <2500 grams. As our tertiary care centre receives referrals from far off places and peripheral health centres, majority of the babies (n=83, 75.5%) were outborn and the rest (n=27, 24.5%) were inborn (Table 1).

Table 1: Demographic details of the study neonates.

Characteristics	Frequency	Percentage
Gender		
Male	65	59.1
Female	45	40.9
Mode of delivery		
NVD	37	33.6
LSCS	73	66.4
Duration of pregnancy (weeks)		
Pre-term (<37)	26	23.6
Term (≥37)	84	76.4
Place of delivery		
Inborn	27	24.5
Out born	83	75.5
Birth weight category (gm)		
≥2500	83	75.5
2499-1500	24	21.8
<1500	3	2.7

In this study, Rh incompatibility (n=40, 36.4%) was the main cause of jaundice in neonates requiring exchange transfusion as shown in Table 2. This was followed by ABO incompatibility (n=22, 20%) and sepsis (n=16, 14.5%). Rh along with ABO incompatibility was present in 13 (11.8%) cases. Cephalhematoma was found in 7 (6.4%) cases.

Table 2: Etiology of neonates with jaundice who underwent DVET.

Aetiology	Number	Percentage
Rh incompatibility	40	36.4
ABO incompatibility	22	20
Sepsis	16	14.5
Rh + ABO incompatibility	13	11.8
Others	12	10.9
Cephalhematoma	7	6.4
Total	110	100

Table 3: Distribution of number of DVET' s done among study subjects.

No. of DVETs done	Frequency	Percentage
1	89	80.9
2	19	17.3
3	2	1.8

More than one double volume exchange transfusion (DVET) was required in 21 (19%) patients. Of these, 19 (90.5%) neonates required twice and 2 (9.5%) neonates required exchange transfusion thrice (Table 3).

The mean age of neonates at admission and mean age at DVET in days were 4.03±2.46 and 4.25±2.44 respectively. The mean birth weight of neonates treated with DVET was found to be 2.81±0.57. The mean total serum bilirubin at pre-exchange and post exchange were 26.13±6.58 mg/dl and 11.63±3.24 mg/dl respectively (Table 4).

Table 4: Description of various continuous variables among study subjects.

Variables	Age at admission (days)	Age at DVET (days)	Birth weight (kg)	Serum bilirubin pre-DVET	Serum bilirubin post-DVET
Mean	4.03	4.25	2.81	26.13	11.63
Median	4.00	4.00	3.00	26.13	11.99
Standard deviation	2.46	2.44	0.57	6.58	3.24
Minimum	1.00	1.00	1.15	13.30	3.31
Maximum	11.00	13.00	4.50	46.00	20.00

DISCUSSION

The objective of this study was to determine clinical profile and the etiology of neonates with severe hyperbilirubinemia who underwent DVET in more than or equal to 35 weeks of gestation.

The percentage of male neonates among those requiring exchange were 59.1% and female neonates were 40.9% with male-to-female ratio of 1.4:1. This was almost identical to the available literature.[12-14] All studies showed male preponderance among neonates with severe hyperbilirubinemia. Hence, male sex has emerged as a well-recognized risk factor for exchange range hyperbilirubinemia in neonates.[15] As our tertiary care centre recieves referrals from far off places and peripheral health centres, majority of the babies (n=83, 75.5%) were outborn and the rest (n=27, 24.5%) were inborn. In this study, we found that LSCS was the common mode of delivery with 66.4% neonates delivered via LSCS. Murki et al and Manning et al reported NVD as the common mode of delivery.[16,17]

In this study, Rh incompatibility was the most common reason for exchange range hyperbilirubinemia present in 40 (36.4%) neonates. Studies by Bhat et al, Davutoğlu et al, Badiee, Dikshit et al, Narang et al, and Chitlangia et al had reported Rh incompatibility in 20.6%, 12.6%, 11.7%, 10.7%, 9.2%, and 6.7%, respectively.[12,13,18-21] Among all the studies our study reflected the highest rate of Rh incompatibilityin neonates reflecting geographical and racial variations.

ABO incompatibility was the second most common reason for exchange transfusion in neonates present in 22 (20%) neonates. Variable incidence of 35.9%, 5%, 25%, 38%, 32%, 22%, and 15% has been reported in available literature.[12,13,18-22] Sepsis was observed in 14.5% (n=160) of the total patients in our study. Narang et al and Dikshit et al have reported the incidence of sepsis in 24% and 8% respectively.[20,21] In our study, Cephalhematoma was observed in 6.4% of the neonates requiring exchange transfusion. Narang et al reported that 1.4% of neonates had cephalhematoma.[21] No cause for exchange range hyperbilirubinemia could be ascertained in 10.9% of the total study patients in our study. Previous studies have reported rates of 9.3% by Dikshit et al, 13.9% by Davutoğlu et al, 27.5% by Chitlangia et al, and 35.4% by Narang et al.[12,13,20,21] The wide variation in the percentage of idiopathic cases can be due to genetic mutations in enzymes involved in bilirubin production and metabolism in addition to the regional differences and resource availability among various studies.

The mean age of presentation in our study was 4.03±2.46, available literature has reported the age of presentation in days as 4±1 days and 4.9±2.2 days.[18,12] The mean birth weight of neonates in our study was 2.81±0.57 kg. Previous studies show mean body weight to be 2.81±0.67 with minimum of 1.2 kg and maximum of 4.3, 2.53±0.52, and 3.36±0.48 kg.[12,14,18] The mean of preexchange TSB level was 26.13±6.58 mg/dl. This was reported to be 30 mg/dl by Bhat et al, 25.9±7.5 mg/dl by Badiee et al, and 28.1±6.4 by Davutoğlu et al.[12,18,19] All these studies showed bilirubin levels >25 mg/dl to be uniformly present in neonates requiring exchange transfusion.

CONCLUSION

Identification of risk factors predisposing to exchange range hyperbilirubinemia and neurotoxicity prediction in healthy near term and term neonates can help in the stratification of high-risk group. Management of neonatal hyperbilirubinemia with strict following of hour based normograms can further result in decrease into morbidity, mortality, and neurotoxicity resulting into neurodevelopmental disorders. In our study, Rh

incompatibility was the most common cause of double volume exchange transfusion.

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