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Original Article

Outcome of outborn Babies Admitted with RH Isoimmunization with Mild-to-Moderate Bilirubin Encephalopathy

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Abstract

Objective: The objective of this study was to study the outcome of outborn babies admitted with Rh isoimmunization with acute bilirubin encephalopathy (ABE).

Patients and Methods: All babies born outside the institute (outborn) admitted with neonatal hyperbilirubinemia were screened for Rh isoimmunization and ABE. Infants with G6PD deficiency were excluded from the study. Babies were followed till discharge. Number of double volume exchanges, age at the first exchange, time taken for the first exchange, number of blood transfusions, and neurological status at discharge were noted in a structured per forma.

Results: A total of 1661 babies were admitted with neonatal jaundice, of which 107 (6.4%) had Rh isoimmunization. 30/107 (28%) babies had mild-to-moderate ABE. All babies underwent double volume exchange transfusion. 20 babies (66%) required the second exchange and only one baby required the third exchange (3.3%). 27 babies (90%) were discharged, of which 20 (74.1%) had intact neurological outcome. 2 (6.7%) babies died due to severe sepsis and 1 (3.3%) left against medical advice. Overall, intact neurological outcome was seen in 66.6% (assuming case of worst case scenario)

Conclusion: The incidence of Rh isoimmunization and ABE is still high in our population. These babies require multiple exchange transfusion during admission. The outcome of the babies in ABE can be improved with prompt intervention.

Key words: Bilirubin, Encephalopathy, Isoimmunization

INTRODUCTION

Rh isoimmunization is one of the preventable neonatal diseases. Anti-D alloantibody is the most common cause of Rh isoimmunization. Before the introduction of anti-D immunoprophylaxis, anti-D immunization affected 1% of neonates and was the cause of death of one in every 2200 babies born.[1] With the advent of anti-D, the incidence in the western world has come down to 0.4 per 1000 live births.[2]

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As compared to western world, the Rh isoimmunization is still common in India. Moreover, due to poor antenatal, perinatal, and neonatal care, the neonates presenting late in acute bilirubin encephalopathy (ABE) are still common. Rh isoimmunized newborns presenting to the health-care facilities are only tip of the iceberg, with may dying *in utero* due to lack of adequate maternal care. Therefore, it is difficult to calculate the true incidence of Rh isoimmunized newborn. Still, hospital surveys serve the purpose of highlighting problem of the preventable disease.

METHODS

The study was conducted in newborn unit of the Department of Pediatrics, Shri Maharaja Gulab Singh Hospital, Jammu (a level 3 newborn care facility in Northern India) over a period of 1 year from April 2015 to March 2016 after taking consent from the Institutes Ethical Committee. All outborn newborn admitted with

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neonatal jaundice were screened for Rh isoimmunization and mild-to-moderate ABE. Rh isoimmunization was defined as "Rh-positive babies born to mother with Rh-negative blood group with positive direct Coombs test." ABE at admission was assessed using BIND score.[3] G6PD deficient neonates were excluded from the study.

Culture positive sepsis (systemic evidence of infection associated with positive blood culture), culture negative clinical sepsis (systemic evidence of infection+negative blood culture + positive sepsis screen (at least one of the following: C-reactive protein>10 mg/L, micro-ESR>10 mm in 1 h, abnormal absolute neutrophil count[4] elevated total leukocyte count and immature: Total neutrophils ratio >0.16).

After taking informed consent, all the characteristics were noted in prestructured per forma. Gestational age was calculated primarily based on mothers last menstrual period (LMP). In cases where LMP was unreliable, either an early dating scan or clinical postnatal assessment by new Ballard score was used to calculate the gestational age. Babies were followed till discharge.

Descriptive statistics were used to describe variables. Mean, median, and mode were used as measures of central tendency depending on the distribution of continuous variable. All analyses were done using IBM-SPSS v.20 and Microsoft Excel. Risk factors for combined outcome of death and abnormal neurological status at discharged were assessed using binary logistic regression.

RESULTS

A total of 1661 neonates with neonatal jaundice were admitted over a period of 1 year, of which Rh isoimmunization was seen in 107 (6.4%). 30 neonates were diagnosed with Rh isoimmunization and ABE with mild-to-moderate severity. Demographic variables are illustrated in Table 1.

Characteristics during the hospital stay are illustrated in Table 2. All babies underwent double volume exchange transfusion and started on double surface phototherapy according to the American Academy of Pediatrics guidelines.[5] 20 babies (66%) required the second exchange and only one baby required the third exchange (3.3%). Median time taken from admission to the first exchange was 8.5 h. No major complications occurred during exchange transfusion.

Two babies developed blood culture-positive sepsis (*Enterococcus faecium* and *Klebsiella pneumonia*). One baby developed NEC Stage IIA. 4 (13.3%) babies required blood transfusion for anemia. 27 babies (90%) were discharged, of which 20 (74.1%) had intact neurological outcome. 2 (6.7%) babies died due to severe sepsis and 1 (3.3%) left against medical advice. Overall, intact neurological outcome was seen in 66.6% (assuming case of worst case scenario).

Risk factors age of admission, admission first exchange interval, and total serum bilirubin at admission (decided *a priori*) were assessed against the combine binary outcome of death and abnormal neurological outcome at discharge and found not be significant [Table 3]. This might be due to small sample size in our study.

DISCUSSION

The study highlights the magnitude of problems in our population. The true incidence of Rh isoimmunization is difficult to assess due to admission and selection bias. Bhutani *et al.* estimated the risk of Rh isoimmunization at 0.36% live birth.[6] The incidence of Rh isoimmunization

Table 1: Baseline characteristics

Mean gestation (in weeks)	38±1.4
Mean weight at admission (in grams)	2872±508
Sex	
Male (%)	23 (76)
Female (%)	7 (23)
Age at admission (in hours) (median IQR)	46 (19–67)
Antenatal ICT titers	
Not done (%)	15 (50)
Positive (%)	15 (50)
Mean serum bilirubin at admission (mg/dl) (mean±SD)	22±5
Mean packed cell volume at admission (%) (mean±SD)	37±4

SD: Standard deviation

Table 2: Characteristics of babies during hospital course

Severity of ABE at admission	
Mild (%)	22/30 (74)
Moderate (%)	8 (26)
Median time taken from admission to exchange in hours (Median-IQR) (%)	8.5 (5–13.5)
Number of double volume exchange transfusion	
Two	20/30 (66)
Three	1/30 (3.3)
Duration of phototherapy (Median-IQR) (hours)	120 (96–120)
Sepsis	
Suspected	19/30 (63)
Proven	2/30 (6.7)
Meningitis	3/30 (10)
NEC (%)	1/30 (3.3)
Median (IQR) duration of hospital stay (in days) (%)	8 (6.7–12)
Outcome	
Discharged (%)	27/30 (90)
Death (%)	2 (6.7)
Left against medical advice (%)	1 (3.3)

ABE: Acute bilirubin encephalopathy

Table 3: Risk factors assessing the combine binary outcome of death and abnormal neurological status at discharge

Risk factor	Odds ratio	95% confidence interval
Age at admission	0.98	0.96–1.01
Total serum bilirubin at admission	0.91	0.74–1.1
Time taken from admission to the first exchange transfusion	0.97	0.83–1.1

as the cause of jaundice was more (6.4%) in our study as compared to the period a study by Narang *et al.* and Cheng *et al.* at 2.9%.[7,8]

The median (IQR) age at admission 47 (19–67) h of these outborn babies is a point of concern. Most of these babies were from the far-flung hilly areas where antenatal, natal, and postnatal care is inadequate. Moreover, it also reflects the shortfalls in transportation of sick newborns.

An important aspect to highlight is the delay in conducting double volume exchange transfusion (median delay of 8.5 h from admission). Rh isoimmunization with ABE is neonatal emergency, and any delay may worsen the neurological outcome. Further, quality improvement studies are required to minimize the delay.

27 (90%) babies were discharged successfully, of which 7 (23.3%) had abnormal neurological outcome at discharge. In a study conducted in Taiwan, only two of 83 babies developed kernicterus.[9] Our results are more consistent with a study by Bhutani *et al.* who estimated the incidence of kernicterus around 13%.[6]

The major shortcoming in our study is that we could not follow-up babies post discharge to know about the long-term outcome. Moreover, our study suffers from admission bias. In spite of these shortcomings, ours study tries to bridge the gap in the knowledge about them magnitude of the problem in the current era. The favorable short-term outcome might still be expected in mild-to-moderate ABE if the treatment is prompt (66.6% of babies had intact neurological outcome at discharge).

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