

**Outcome of exchange transfusion for hyperbilirubinemia among term neonates in nicu of a tertiary care centre.**

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**Abstract**

**Introduction:** Hyperbilirubinemia remains a common reason for hospital admission during the neonatal period. Severe hyperbilirubinemia in neonates can lead to acute bilirubin encephalopathy or permanent neurological sequelae in survivor. Kernicterus or bilirubin encephalopathy is caused by unconjugated hyperbilirubinemia that develops either as a result of hemolytic process or because of the inability of the liver to conjugate bilirubin. The risk of mortality and severe long-term neurological sequelae due to severe hyperbilirubinemia is high. This study includes all the neonates admitted in tertiary care hospital undergoing exchange transfusion in past 2 years.

**Aims and objectives:** To determine the outcome and side effects of exchange transfusion in term neonates to study the risk factors in neonates and maternal risk factors resulting in hyperbilirubinemia requiring exchange transfusion.

**Methodology:** The study was carried out in nicu of our institute. Blood grouping and Rh typing were done for both mothers and newborns. In all newborns, pre-exchange complete blood count, peripheral blood film,

Coombs test, reticulocyte count, serum bilirubin and post-exchange serum bilirubin, haemoglobin was done. Frequency, maternal and neonatal factors, indications, and outcomes were analyzed.

**Result:** It was observed that neonates requiring exchange transfusion were mostly term associated more commonly with rh incompatibility.

**Conclusion:** Exchange transfusion was required among few of the admitted newborns with unconjugated hyperbilirubinemia. The common adverse effect is sepsis. The commonest indication was Rh incompatibility. Overall outcome after exchange transfusion was favorable.

**Introduction**

Jaundice is one of the most common conditions requiring medical attention in newborn babies. Approximately 60% of term and 80% of preterm babies develop jaundice in the first week of life, and about 10% of breastfed babies are still jaundiced at 1 month of age.<sup>1</sup> While severe hyperbilirubinemia (total serum bilirubin [TSB] level of >20 mg/dL [342.1 µmol/L]) occurs in 30 mg/Dl.<sup>4,5</sup> Some of the common causes of neonatal jaundice include physiological jaundice, breast feeding or non-feeding

jaundice, breast milk jaundice, prematurity leading to jaundice and various pathological causes like hemolytic disease, liver dysfunction, neonatal sepsis, deficiency of glucose – 6 - phosphatase (G6PD) enzyme, Rh-in compatibility, hypothyroidism and rare conditions such as Gilbert's syndrome, Crigler-Najjar syndrome etc.<sup>6,7</sup>

Bilirubin inhibits mitochondrial enzymes, interferes with DNA and protein synthesis<sup>6</sup>, and alters cerebral glucose metabolism<sup>4</sup>. Unconjugated bilirubin initiates a Mitochondrial pathway of apoptosis in developing brain neurons and it inhibits the function of N-methyl-aspartate-receptor ion channels.<sup>8</sup> The region most commonly affected are the basal ganglia, particularly the sub-thalamic nucleus and the globus pallidus, the hippocampus, the geniculate bodies, various brainstem nuclei, including the inferior colliculus, oculomotor, vestibular, cochlear, and inferior olivary nuclei, and the cerebellum especially the dentate nucleus and the vermis.<sup>9</sup>

Kernicterus or bilirubin encephalopathy is caused by unconjugated hyperbilirubinemia that develops either as a result of hemolytic process or because of the inability of the liver to conjugate bilirubin.<sup>10,11</sup>

Kernicterus is preventable through the use of phototherapy, treatment with intravenous immunoglobulins (IVIg), or the use of exchange transfusion (ET) to lower serum bilirubin levels.<sup>12</sup> Despite proven benefit, exchange transfusion might give rise to cardiovascular, biochemical, or hematological complications and mortality rates vary from 0.5 to 3.3%.<sup>2</sup> Thus, current recommendation for exchange transfusion is based on seeking a balance between risk and benefit.<sup>13,14</sup> Moreover, the introduction of anti-Rh (D)-specific immunoglobulin, intrauterine transfusions, prenatal monitoring, high-intensity phototherapies, and the use of non-specific human immunoglobulin have made considerable contributions to reducing the indications for ET.<sup>15-18</sup>

In hemolytic disease, immediate exchange is needed when 1. Cord bilirubin level >4.5mg/dl and cord haemoglobin level 1mg/dl despite phototherapy. 3. Haemoglobin level is between 11g/dl and 13g/dl, and bilirubin level is rising >0.5mg/dl despite phototherapy. 4. Bilirubin level is 20mg/dl or appears to reach 20 mg/dl at the rate it is rising. 5. There is progression of anaemia in face of adequate control of bilirubin by other methods.<sup>1</sup>

The bilirubin level at which intervention is necessary and its outcome is still a contentious issue. Hence in the present study we aimed to study outcome of exchange transfusion for hyperbilirubinemia among term neonates in NICU of a tertiary care centre.

### Aims & objectives

- 1) To determine the outcome and side effects of exchange transfusion in term neonates
- 2) To study the risk factors in neonates and maternal risk factors resulting in hyperbilirubinemia requiring exchange transfusion.

### Material & methods

In the present study, 160 patients were enrolled prospectively over 2 years of study period from October 2020 to October 2022. Detailed patient information was taken at the time of admission in NICU. Study was done in Department of Pediatrics, SRTR Government Medical College, Ambajogai, dist. Beed, Maharashtra, India, after getting informed consent from parents. Study was approved by institutional Ethics Committee. In this study 160 term and near-term neonates who underwent exchange transfusion for significant unconjugated hyperbilirubinemia were included. Neonates undergoing exchange transfusion due to causes other than hyperbilirubinemia were not included in study.

### Study Procedure

Cord blood investigations in the setting of Rh incompatibility were sent. In the probable ABO setting,

ABO blood grouping, Rh typing, serum bilirubin, complete blood count, reticulocyte count, and Comb's tests were sent from peripheral blood. In suspected case of sepsis, septic workup was done as per unit protocol. Glucose – 6 - phosphate dehydrogenase deficiency (G6 PDH) and minor blood grouping were done whenever suspected.

All patients were given phototherapy before and after the procedure. Small amount of blood (5 mL/kg) was exchanged in each pass using the pull and push technique.

Each pass (starting from the drawing of the baby's blood per UVC, disposing of that old blood, followed by drawing donor blood and transfusing that blood into the infant) takes approximately 1.5 to 2 minutes for completion. Vital signs including SpO2 were monitored continuously during the procedure, 4 hourly for 24 hours and 8 hourly thereafter. Any complications that were not present before DVET and occurred during and within 3 days after the exchange. Complications observed were taken into consideration for immediate intervention.

All infants who were included in study were followed at regular interval up to 12 months of age.

BERA was done at 3 months of age, follow up and assessment during later period (6 months and 12 months) was done in terms of attainment of neurodevelopmental milestone.

Data was entered in excel sheet, cleaned and coded. Percentages were computed for categorical variables. Comparison was done by unpaired student t- test with the help of SPSS software.

**Results**

During the duration of two years of study, total 160 newborn were enrolled.

Table 1: Distribution of study subjects according to variables.

Variable	Frequency	Percentage	
Gender	Male	86	54
	Female	74	46
Birth weight	LBW	89	56
	Normal	71	44
Gestational Age	Term	64	40
	Late Term	96	60
Mode of Delivery	NVD	138	86
	LSCS	22	14
Age of onset of jaundice	<24 hrs	142	89
	24 to 72 hrs	18	11

Graph 1: Distribution of study subjects according to variables.

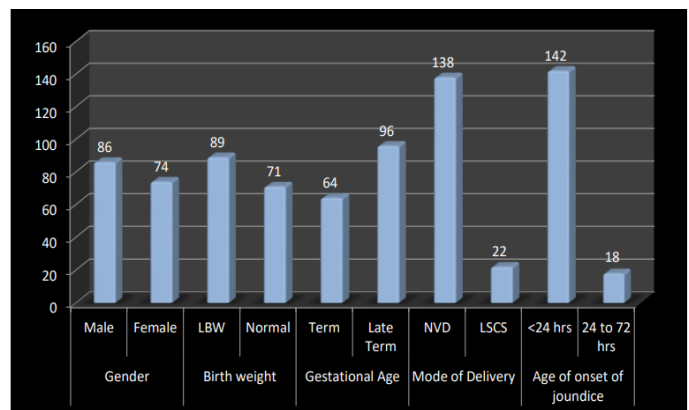


Table 2: Distribution of study subjects according to etiology.

Etiology	Frequency	Percentage (%)
Rh incompatibility	142	89
ABO incompatibility	8	5
Minor blood group incompatibility	2	1
Hyperbilirubinemia in IDM (no other cause specified)	3	2
G6PDH deficiency	2	1
Exaggerated physiological jaundice	3	2

Graph 2: Distribution of study subjects according to etiology.

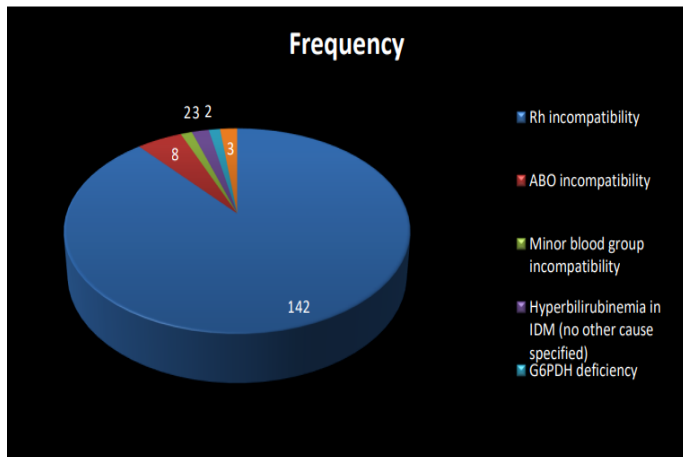


Table 3: Distribution of study subjects according to adverse events.

Adverse Events	Frequency	Percentage (%)
Hyperglycemia	86	54
Sepsis following exchange transfusion	27	17
Anemia requiring top-up transfusion	34	21
Hypocalcemia	21	13
Thrombocytopenia	10	6
Catheter-related complications	2	1

Graph 3: Distribution of study subjects according to adverse events.

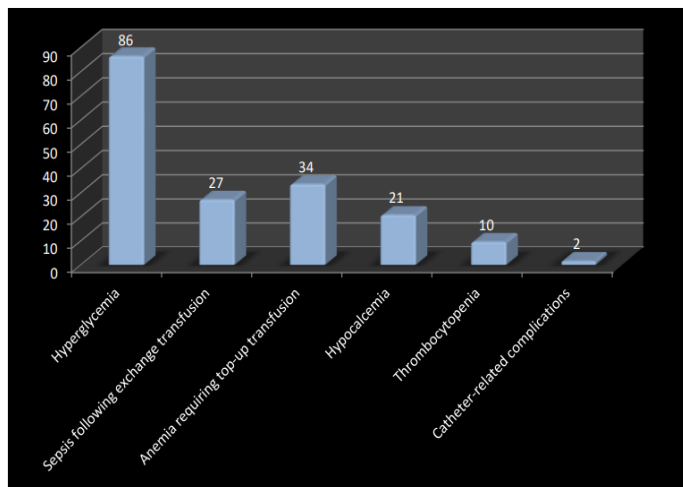
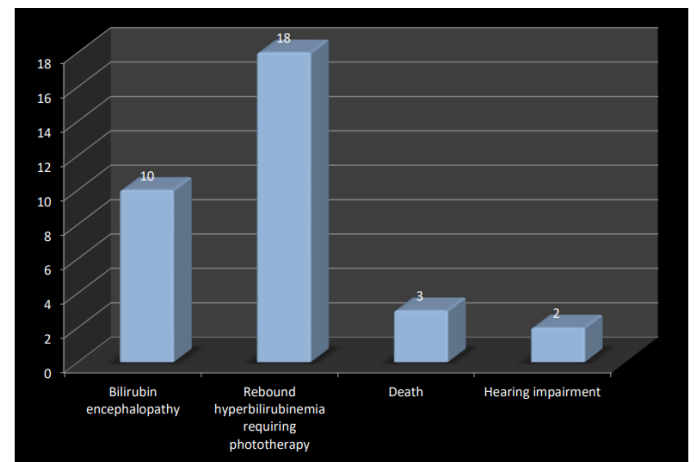


Table 4: Distribution of study subjects according to outcome.

Outcome	Frequency	Percentage (%)
Bilirubin encephalopathy	10	6
Rebound hyperbilirubinemia requiring phototherapy	18	11
Death	3	2
Hearing impairment	2	1

Graph 4: Distribution of study subjects according to outcome.



### Discussion

In the present study we included 86 (54%) male and 74 (46%) female patients. Out of the study subjects 71 were with normal and 89 were with low birth weight. 56 babies were born in pre term 37 were in term and 67 were in late term. Normal vaginal delivery occurred in 138 patients while LSCS was done in 22 patients. In the 142 patients age of onset of jaundice was below 24 hours while in 18 patients it was started in between 24 to 72 hours. Similar findings were seen in the study done by Dey s et al, Arpit K et al.

Among study subjects 142 (89%) were with Rh in compatibility, 8 (5%) were with ABO incompatibility, 2 (%) were with minor blood group incompatibility, 3 (%) were with hyperbilirubinemia in IDM (no other cause

specified), 2 (1%) were with G6PDH deficiency while 3 (2%) patients were with exaggerated physiological jaundice. Dey s et al in their study mentioned that more than three-fourth of babies (33/41, 80.5%) requiring exchange transfusion had Rh incompatibility, and four babies (9.8%) had ABO incompatibility. The remaining four patients were diagnosed with minor blood group incompatibility, hyper bilirubinemia in an infant of diabetic mother where no other cause could be identified, G6PD deficiency, and exaggerated physiological jaundice. Arpit K et al in their study found that study most common cause of hyperbilirubinemia requiring exchange transfusion was ABO incompatibility i.e 42. 86%, (n=15). Rh incompatibility constituted 22. 85% of cases (n=8). In remaining 34.29% cases (n=12) no specific cause could be found.

Adverse events like hyperglycemia seen in 54%, sepsis in 17%, anemia in 21%, hypocalcemia in 13%, thrombocytopenia in 6% while catheter related complications seen in 1% study cases. Dey s et al stated that the most common complication related to the exchange transfusion was hyperglycemia (51.2%). Next to hyperglycemia, sepsis following exchange transfusion was the second most common complication found in 19.5% of newborns. Anemia requiring top-up transfusion and hypocalcemia were found in 17.1 and 14.6%, respectively. There were no catheter-related complications. Among the study subjects bilirubin encephalopathy was seen in 10 patients, rebound hyperbilirubinemia requiring phototherapy was seen in 18 patients, hearing impairment was seen in 2 patients while death occurred of 3 patients after ET. Arpit K et al in their study observed that no mortality occurred in our study. None of the enrolled neonate had to undergo repeat exchange transfusion. It is comparable to study conducted by Sanpavat S8 where morbidity was noted in 15.3% of cases. Badee Z9 also found com

plication in 14 neonates (20.9%) in his study. Patra K7 et al showed higher incidence (74%) of associated abnormalities, com monest being thrombocytopenia (44%) followed by hypocalcemia (29%).

### Conclusion

Rapidly increasing bilirubin levels in neonates is very harmful for neonates and may be life threatening if not treated promptly. Age of onset of jaundice is below 24 hours in most of cases. Rh incompatibility and ABO incompatibility are the most common indication of exchange transfusion. Hyperglycemia, sepsis and anemia are the common adverse event occurred during ET. Exchange transfusion is one of the most effective and safe method of treating NNH.

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