

Frequency of Common Causes of Severe Hyperbilirubinemia in Neonates Leading to Exchange Transfusion

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1. Abstract

1.1. Introduction: Severe hyperbilirubinemia can cause neurotoxicity called kernicterus which is a neurological syndrome resulting from the deposition of unconjugated bilirubin in the basal ganglia and brainstem nuclei due to which patients suffer from long term morbidities consisting of developmental delays, sensorineural hearing loss, mental retardation and other significant brain damage [1]. Acute neurotoxicity can cause poor feeding, lethargy then irritability and high pitched cry and arching back may appear [1]. Kernicterus develops in 30 percent of infants (all gestational ages) with untreated hemolytic disease and bilirubin levels more than 25-30 mg/dl. Overt neurologic signs have a grave prognosis; more than 75% of infants die, and 80% of affected survivors have bilateral choreoathetosis with involuntary muscle spasms [1]. This descriptive cross sectional study performed with reviewing of files of 187 neonates who had exchange transfusion in special care baby unit Khyber teaching hospital Peshawar from June 2018 to Dec 2019.

1.2. Results: In this study mean age was 5 days with standard deviation ± 2.62 . Sixty four percent neonates were male and 36% neonates were female. Thirty eight percent neonates had ABO incompatibility, 18% neonates had RH incompatibility, 15% neonates had G6PD deficiency, and 10% neonates had sepsis.

1.3. Conclusion: Our study concludes that the most common cause of severe hyperbilirubinemia in neonates leading to exchange transfusion was ABO incompatibility (38%) followed by RH incompatibility (18%), G6PD deficiency (15%) and sepsis (10%).

2. Introduction

Severe hyperbilirubinemia can cause neurotoxicity called kernicterus which is a neurological syndrome resulting from the deposition of unconjugated bilirubin in the basal ganglia and brainstem nuclei due to which patients suffer from long term morbidities consisting of developmental delays, sensorineural hearing loss, mental retardation and other significant brain damage [1]. Acute neurotoxicity can cause poor feeding, lethargy then irritability and high pitched cry and arching back may appear [1]. Kernicterus develops in 30 percent of infants (all gestational ages) with untreated hemolytic disease and bilirubin levels more than 25 -30 mg/dl. Overt neurologic signs have a grave prognosis; more than 75% of infants die, and 80% of affected survivors have bilateral choreoathetosis with involuntary muscle spasms [1]. To avoid from bilirubin encephalopathy immediate phototherapy [2] is started but the effect of phototherapy is variable because of difference in light source and configuration in such case we must proceed to exchange transfusion which remains a frequent emergency procedure in many developing countries [3].

Unconjugated hyperbilirubinemia occurs because of increased bilirubin production (hemolytic anemia, polycythemia, cephalhematoma/bruising,); factors that reduce the activity of the transferase enzyme (genetic deficiency, hypoxia, infection, thyroid deficiency, drugs) or defective bilirubin clearance from blood [4].

2.1. Objective

To determine the frequency of common causes of severe hyperbilirubinemia in neonates leading to exchange transfusion.

2.2. Operational Definitions

2.2.1. Neonate: Those neonates (first 28 days after birth) who have indirect hyperbilirubinemia, weighting 2 kg or more and are candidates for exchange transfusion.

2.2.2. Gestational Age: The term used for duration of pregnancy, measured in weeks from day of a woman's last menstrual cycle to current date or till birth. Gestational age 35 to 42 weeks will be included in the study.

2.2.3. Severe Hyperbilirubinemia: Serum bilirubin level coming in the range of exchange transfusion according to guideline tables printed in Nelsons text book of pediatrics will be considered as severe hyperbilirubinemia.

Exchange transfusion: Defined as the procedure by which baby blood will be removed and replaced with donor blood performed via umbilical vein catheterization.

3. Material and Methods

Study Setting: Special care baby unit Dept. of child health, Khyber Teaching Hospital, Peshawar.

Study Design: Cross sectional descriptive study.

Duration: Six months (16/6/2018 to 16/12/2019).

Sample Size: A total of 187 patients were observed by using 8.5% proportion of sepsis, 95% confidence interval and 4% margin of error with the help of WHO software for sample size determination.

Sample Technique: Non probability consecutive sampling.

Inclusion Criteria:

- AGE; first 28 days of life.
- Both genders.
- GESTATIONAL AGE: Neonates with gestational age 35 to 42 weeks were included in the study.
- Babies with severe hyperbilirubinemia leading to exchange transfusion (according to guideline tables printed in Nelsons text book of pediatrics.)

Exclusion Criteria:

- Babies weighting less than 2 kg.
- Babies with congenital anomalies.
- Asphyxiated babies.
- Disseminated intra vascular coagulation.
- Metabolic causes; galactosemia, hypothyroidism.

Justification: All the above factors are confounders and had made the study results biased if included.

3.1. Data Collection Procedure

For every patient included in the study a detailed history was noted with special emphasis on age of baby in days/hours, gestational age in weeks. Patients admitted with signs and symptoms of

jaundice, meeting the inclusion criteria had included in the study. The purpose and benefits of study was explained to patients and informed consent was obtained. Similarly, detailed history and examination with special emphasis on signs and symptoms of sepsis. The following investigations were performed for every included baby in the study. Complete Blood Counts, Retic Count, Coombs Test (Direct), Baby Blood Group, Mother blood Group, Serum Bilirubin Total Direct and Indirect and blood culture. G6PD qualitative screening test. With the help of above mentioned information the common causes of severe neonatal hyperbilirubinemia that leads to exchange transfusion was determined and recorded in the Performa (appendix 1). Strict exclusion criteria had followed to control confounders and bias in the study results.

3.2. Data Analysis

Data was collected by Performa and was analyzed in SPSS version 16 or 17. Frequencies and percentages were calculated for categorical variables like gender, causes of severe hyperbilirubinemia leading to exchange transfusion. Mean and standard deviation was calculated for continuous variables like age of baby, gestational age, serum bilirubin, retic count. The common causes were stratified among age and gender to see the effect of modification. Post stratification was done through Chi-square test, keeping P value ≤ 0.05 significant. All the results were presented in graphs and charts.

4. Results

This study was conducted at Department of Pediatrics Medicine, Khyber Teaching Hospital, Peshawar in which a total of 187 patients were observed to determine the frequency of common causes of severe hyperbilirubinemia in neonates leading to exchange transfusion and the results were analyzed as:

Age distribution among 187 neonates was analyzed as 135(72%) neonates were in age range 2-5 days, 41(22%) neonates were in age range 6-10 days and 11(6%) neonates were in age range 11-14 days. Mean age was 5 days with standard deviation ± 2.62 .

Gender distribution among 187 neonates was analyzed as 120(64%) neonates were male and 67(36%) neonates were female.

Period of gestation among 187 mothers was analyzed as 116(62%) mother had POG ≤ 37 weeks while 71(38%) mother had POG >37 weeks.

Serum Bilirubin (SBR) level before exchange transfusion was analyzed as 127(68%) neonates had serum bilirubin level ranged 25-30mg/dl while 60(32%) neonates had serum bilirubin level ranged 31-35 mg/dl. Mean serum bilirubin was 27.83 mg/dl with standard deviation ± 16.71 .

Retic count was analyzed as 112(60%) neonates had retic count ranged 2%-3% while 75(40%) neonates had retic count ranged 4%-5%. Mean retic count was 3 with standard deviation ± 1.27 .

Causes of severe hyperbilirubinemia were analyzed as 71(38%)

neonates had ABO incompatibility, 34(18%) neonates had RH incompatibility, 28(15%) neonates had G6PD deficiency, and 19 (10%) neonates had sepsis.

Stratification of causes of severe hyperbilirubinemia with respect to age and gender is given in (Table 1, 2).

Table 1: Stratification of causes of severe hyperbilirubinemia w.r.t age distribution (n=187)

CAUSES		2-5 days	6-10 days	11-15 days	Total	P value
ABO INCOMPATIBILITY	Yes	51	16	4	71	0.471
	No	84	25	7	116	
Total		135	41	11	187	
RH INCOMPATIBILITY	Yes	24	8	2	34	0.402
	No	111	33	9	153	
Total		135	41	11	187	
G6PD DEFICIENCY	Yes	20	6	2	28	0.398
	No	115	35	9	159	
Total		135	41	11	187	
SEPSIS	Yes	14	4	1	19	0.377
	No	121	37	10	168	
Total		135	41	11	187	

Table 2: stratification of causes of severe hyperbilirubinemia w.r.t gender distribution (n=187)

CAUSES		Male	Female	Total	P value
ABO INCOMPATIBILITY	Yes	45	26	71	0.272
	No	75	41	116	
Total		120	67	187	
RH INCOMPATIBILITY	Yes	22	12	34	0.263
	No	98	55	153	
Total		120	67	187	
G6PD DEFICIENCY	Yes	28	0	28	0.011
	No	92	67	159	
Total		120	67	187	
SEPSIS	Yes	12	7	19	0.291
	No	108	60	168	
Total		120	67	187	

5. Discussion

Severe hyperbilirubinemia can cause neurotoxicity called kernicterus which is a neurological syndrome resulting from the deposition of unconjugated bilirubin in the basal ganglia and brainstem nuclei due to which patients suffer from long term morbidities consisting of developmental delays, sensorineural hearing loss, mental retardation and other significant brain damage [1]. Acute neurotoxicity can cause poor feeding, lethargy then irritability and high pitched cry and arching back may appear [1]. Kernicterus develops in 30 percent of infants (all gestational ages) with untreated hemolytic disease and bilirubin levels more than 25 -30 mg/dl. Overt neurologic signs have a grave prognosis; more than 75% of infants die, and 80% of affected survivors have bilateral choreoathetosis with involuntary muscle spasms [1]. To avoid from bilirubin encephalopathy immediate phototherapy [2] is started but the effect of phototherapy is variable because of difference in light source and configuration in such case we must proceed to exchange transfusion which remains a frequent emergency procedure in many developing countries [3].

Our study shows that mean age was 5 days with standard deviation ± 2.62 . Sixty four percent neonates were male and 36% neonates were female. Mean serum bilirubin was 27.83 mg/dl with standard deviation ± 16.71 while mean retic count was 3 with standard deviation ± 1.27 . Causes of severe hyperbilirubinemia were analyzed as 38% neonates had ABO incompatibility, 18% neonates had RH incompatibility, 15% neonates had G6PD deficiency, and 10% neonates had sepsis.

Similar findings were observed in another study conducted Farhad Heydrian et al [5] in Iran in which a total of 118 patients were observed in which 75(63.6%) were male and 43 patients (36.4%) were female. More over ABO incompatibility was a major cause of exchange transfusion (38.1%) unknown etiology (25.4%) RH incompatibility (16.1%) sepsis (8.5%).

Similar findings were observed in another study conducted Michael Wkuzniewicz et al6 in which Rh in compatibility as a leading cause of hazardous hyperbilirubinemia, when the etiology was identified but in 70% cases etiology was not identified.

Similar findings were observed in another study conducted Alizadeh Taheri et al [7] in Iran in which major causes of exchange transfusion were premature labor (63%) breast feeding jaundice (35%) ABO incompatibility (24.5%) and G6PD (12.8%).

In other studies conducted by Gamaleldin R et al [8] and Bhutani VK et al [9] common causes of neurotoxicity in neonates with severe hyperbilirubinemia were ABO, Rh incompatibility, sepsis, and idiopathic. The frequency of common causes of severe indirect hyperbilirubinemia needs to be determined.

6. Conclusion

Our study concludes that the most common cause of severe hyperbilirubinemia in neonates leading to exchange transfusion was ABO incompatibility (38%) followed by RH incompatibility (18%), G6PD deficiency (15%) and sepsis (10%). Hence early workup for neonatal jaundice can limit the rate of exchange transfusion and prevent the child from the agony.

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