ORIGINAL ARTICLE

CLINICAL PROFILE AND OUTCOME OF TERM AND PRETERM NEWBORNS WITH HYPERBILIRUBINEMIA ADMITTED IN SNCU OF A TEACHING HOSPITAL

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ABSTRACT: Hyperbilirubinemia is the most common clinical condition requiring close attention and monitoring to prevent encephalopathy especially in preterm babies **AIMS:** To study the incidence and causes of neonatal hyperbilirubinemia, to study the risk factors associated with neonatal hyperbilirubinemia, to study the outcome of neonatal hyperbilirubinemia. **METHODS:** The prospective study was conducted at SNCU, Government General Hospital of Kurnool over a period of one year January 2012 to December 2012. Total 160 cases were studied during this period. **RESULTS:** Of the 160 cases, 93(58.12%) were term babies and 67(41.88%) were preterm babies. 78(48.76%) case the cause is physiological jaundice. Rh hemolysis (22.62±2.4mg/dl) followed by ABO hemolysis (20.3±2.6 mg/dl). Out of 160 cases only 4 cases died of causes unrelated to jaundice. Two were due to extremely low birth weight, 1 case due to septicemia and 1 case due to birth asphyxia.

INTRODUCTION: Hyperbilirubinemia is the most common clinical condition requiring evaluation and treatment in the new born.[1] Jaundice is observed during the 1st week of life in approximately 60% of term infants and 80% of preterm infants.[2]

Neonatal jaundice is divided into physiological and pathological categories depending on age of onset, severity, evolution and associated risk factors.[3]

On review of this common problem, it is known that there is a long list of factors which influence the risk of hyperbilirubinemia in the newborns. Some of these factors such as maternal age, labour induction with oxytocin, maternal diabetes, male sex, prematurity; birth asphyxia and neonatal sepsis are known to predispose to hyperbilirubinemia in neonates.[3] Biophysical handicaps that result in jaundice are worse among prematurely born infants thus resulting in greater incidence and severity of jaundice among them.[4]

The importance of jaundice lies in its potential for causing bilirubin encephalopathy in newborns. Acute bilirubin encephalopathy may develop during hazardous hyperbilirubinemia and evolve into chronic adverse neuro developmental sequelae of kernicterus. It is associated with grave morbidity and mortality. Survivors are left with severe neurological handicaps like cerebral palsy (choreoathetoid type), gaze palsies, deafness and other cranial nerve palsies. Kernicterus though preventable, is irreversible.[1]

The incidence of neonatal jaundice is increasing day by day. Hence the present study is undertaken to evaluate causes, risk factors and treatment modalities of neonatal hyperbilirubinemia admitted to SNCU, GGH, Kurnool and focuses specially on hyperbilirubinemia in pre terms.

AIMS OF THE STUDY:

1. To study the incidence and causes of neonatal hyperbilirubinemia.
2. To study the risk factors associated with neonatal hyperbilirubinemia.
3. To study the outcome of neonatal hyperbilirubinemia.

MATERIALS AND METHODS: The prospective study was conducted at SNCU, Government General Hospital of Kurnool over a period of one year January 2012 to December 2012. Total 160 cases were studied during this period.

INCLUSION CRITERIA: Neonates with jaundice delivered inside or outside the Institute, admitted into NICU.

During study period, Neonates with serum bilirubin more than 10 mg/dL, those willing to participate in the study were included.

EXCLUSION CRITERIA: Babies attending outpatient department only, Babies who went discharge against medical advice. Babies whose parents refused consent to participate in the study, Babies above 28 days of age.

METHODS: Jaundice was ascertained by clinical methods and was confirmed by biochemical methods. In babies suspected to have jaundice bilirubin estimation is done first by transcutaneous bilirubinometry. If values found above normal limits serum bilirubin levels estimated.

Serum bilirubin estimation was done by Van den Bergh method. The babies with serum bilirubin more than 10 mg/dL were included in the study. Detailed antenatal, natal and postnatal history was obtained. Thorough clinical examination of every baby was done and all the necessary investigations such as Haemoglobin percentage (Sahli's method), peripheral smear, reticulocyte count, Serum bilirubin (total, direct, indirect), blood grouping and Rh typing of baby and mother, Coomb's test – direct and indirect, VDRL, TORCH titre and T3, T4 & TSH levels. X–ray chest done as per necessity. Serum bilirubin level was repeated, as per requirement.

Treatment for hyperbilirubinemia was carried out as per the guidelines laid down by American Academy of Pediatrics. By phototherapy, drug therapy and exchange transfusion.

Statistical analysis: Since there was no comparative group in the study, results were expressed as ratios and percentages.

Observations:

- **Source:** Government General Hospital, Kurnool.
- **Period of study:** January 2012 to December 2012.
- **Number of patients:** 160.
- **Incidence of Neonatal Hyperbilirubinemia:** A total of 2391 new born babies were admitted to SNCU, Government General Hospital of Kurnool during the study period.

Among them 160 new born babies diagnosed to have neonatal hyperbilirubinemia with incidence is 6.7% of admissions to SNCU.

- **Sex distribution:** Among the 160 new borns with neonatal hyperbilirubinemia, 90(56.25%) were male and 70(43.75%) were female.

Sex	Number (n=160)	Percentage
Male	90	56.25
Female	70	43.75

Table 1: Sexwise distribution of neonates with hyperbilirubinemia

Distribution of cases according to gestational age and sex: Of the 160 cases, 93(58.12%) were term babies and 67(41.88%) were preterm babies. Of the preterm babies, 20(12.5%) were between 33 to 36 weeks gestational age and 20(12.5%) were between 31 to 32 weeks and 27(16.8%) were between 28 to 30 weeks.

Average gestational age at presentation is 34.96 weeks. Prematurity is a significant risk factor for development of neonatal hyperbilirubinemia.

Sl.	Gestational Age	Number	Percentage	Male (%)	Female (%)
1	>37 weeks	93	58.12	57(61.3)	36(38.7)
2	33-36 weeks	20	12.5	9(45)	11(55)
3	31-32 weeks	20	12.5	10(50)	10(50)
4	28-30 weeks	27	16.88	14(51.8)	13(41.2)
	Total	160	100	90(56)	70(44)

Table 2: Distribution of neonates according to gestational age

Distribution of cases according to birth weight: Of the 160 cases, majority were having birth weight more than 2.5 kg. 18 cases were having birth weight more than 3000 grams. 40 cases were having birth weight from 2501 to 3000 grams. 31 cases were having birth weight from 2001 to 2500 grams. 20 cases were having birth weight from 1501 to 2000 grams. 49 cases were having birth weight from 1001 to 1500 grams. 2 cases were having birth weight less than 1000 grams.

Sl. No.	Birth Weight (grams)	Number	Percentage
1	>3000	18	11.25
2	2501-3000	40	25
3	2001-2500	31	19.37
4	1501-2000	20	12.5
5	1001-1500	49	30.625
6	<1000	2	1.25
	Total	**160**	**100**

Table 3: Distribution of neonates depending upon birth weight

Causes and Factors Aggravating Neonatal Hyperbilirubinemia: Of the 160 cases, 156(97.5%) cases were of unconjugated hyperbilirubinemia and 4(2.5%) cases were of persistent conjugated hyperbilirubinemia. 10(6.25%) cases were due to Rh- hemolysis, of which one baby was premature.

27(16.87%) cases were due to ABO –hemolysis, of which 5 were preterm. 34(21.25%) cases were due to septicemia, of which 19 were preterm, 3 had birth asphyxia, 3 were IUGR and 8 had respiratory distress.

In most of the cases, in 78(48.76%) case the cause is physiological jaundice. Persistent conjugated hyperbilirubinemia occurred in 4(2.5%) cases of which 1 is extra hepatic biliary atresia, 2 were neonatal hepatitis and 1 was galactosemia.

Sl. No.	Causes	No. of cases (%)	AGGRAVATING FACTORS		
			Birth asphyxia (%)	Prematurity (%)	IUGR (%)
1	Physiological	78(48.76)	8(10.25)	41(52.5)	5(6.41)
2	Septicemia	34(21.25)	3(8.82)	19(55.88)	3(8.82)
3	ABO - Haemolysis	27(16.88)	-	5(18.51)	-
4	Rh – haemolysis	10(6.25)	-	2(20)	-
5	Birth injuries	7(4.37)	1(14.2)	-	-
6	Neonatal hepatitis	2(1.25)	-	-	
7	EHBA	1(0.62)	-	-	-
8	Galactosemia	1(0.62)	-	-	-
TOTAL		**160(100)**	**12(7.5)**	**67(41.87)**	**8(5)**

Table 4: Causative and aggravating factors

Time of onset of clinical jaundice: Rh and ABO hemolytic jaundice presented early at 23.0±7.39 hours and 37±1.73 hours respectively and this was statistically significant when compared to physiological group (62.80±18.57 hours) with $p< 0.001$.

Prematurity and septicemia presented late with jaundice, at 89.5±13.24 hours and 81.0±26.71 hours respectively and this was also statistically significant when compared with physiological group ($p<0.005$).

Sl. No.	CAUSE OR AGGRAVATING FACTOR (n)	MEAN HOURS OF ONSET	RANGE (HOURS)
1.	Physiological (78)	62.80±18.57	36-94
2.	Rh haemolysis (10)	23±7.39	20-36
3.	ABO haemolysis (27)	37±1.732	36-40
4.	Prematurity(67)	89.5±13.21	70-120

5.	Septicemia (34)	81.0±26.21	40-120
6.	Asphyxia (12)	66.15±13.37	40-90
7.	Birth injuries(7)	60.6±16.07	40-78

Table 5: Showing time of onset of clinical jaundice

Peak serum bilirubin values achieved due to various causes of hyperbilirubinemia:

Rh hemolysis (22.62±2.4mg/dl) followed by ABO hemolysis (20.3±2.6 mg/dl). In these diseases peak serum bilirubin values were attained earlier than other causes: Rh hemolysis -49± 12 hours and ABO hemolysis -65± 17 hours ($p<0.001$).

Peak serum bilirubin values attained in septicemia are lowest – 15.3 ± 1.9 mg/dl ($p<0.05$)

In premature babies age of attainment of peak serum bilirubin level was longer than other causes – 101 ± 12.2 hours ($p<0.05$)

SL NO.	CAUSE/AGGRAVATING FACTORS (NO)	PEAK SERUM BILIRUBIN LEVELS(mg/dl)	AGE OF ATTAINMENT OF PEAK LEVELS(HRS)
1.	Physiological (78)	17.1±2.1	92±11.0
2.	Rh haemolysis (10)	22.62±2.4	49±12.0
3.	ABO haemolysis (27)	20.3±2.6	65±17.0
4.	Septicaemia (34)	15.3±1.9	86.5±10.6
5.	Prematurity (67)	16.42±3.9	101±12.2
6.	Birth asphyxia (12)	17.9±2.6	92±8.6
7.	Birth injuries (7)	16.9±3.6	82.2±12.6

Table 6: Peak serum bilirubin levels according to cause & aggravating factors

Sl. No.	CAUSE/AGGRAVATING FACTOR	MEAN DURATION OF PHOTOTHERAPY (HOURS)	RATE OF FALL OF SERUM BILIRUBIN(mg/dl/day)
1	Physiological (78)	31.8±7.8	1.56±0.32
2	Rh hemolysis (10)	115±5.0	2.38±1.22
3	ABO hemolysis (27)	81±23.0	1.80±1.08
4	Septicemia (34)	34.2±11.5	1.40±0.19
5	Birth injuries (7)	69.6±25.1	1.21±0.22

6	Birth asphyxia (12)	65±29.51	1.26±0.36
7	Prematurity (67)	52.67±22.91	1.44±0.35

Table 7: Mean duration of phototherapy and their statistical significance with comparison to physiological group

Exchange transfusion: Double volume exchange transfusion was done in 14 cases of which 5 cases due to Rh hemolysis, 4 cases due to ABO hemolysis, 4 cases in preterm due to physiological cause and 1 case due to birth injury. In all case exchange transfusion was done only one time only.

Outcome: Out of 160 cases only 4 cases died of causes unrelated to jaundice. Two were due to extremely low birth weight, 1 case due to septicemia and 1 case due to birth asphyxia.

All other cases recovered uneventfully.

DISCUSSION: In the present study the incidence of neonatal hyperbilirubinemia was found to be 6.7% which is similar to Anil Narang et al.[5] reported and Singhal et al.[6] in contrast wit. Henny Harry et al[7] reported the incidence to be 4.6 %.

Sex Distribution: Neonatal hyperbilirubinemia was more common in male babies compared to female babies. In the present study 90(56.25%) were male babies and 70(43.75%) were female babies similar to with Narang et al.[5] and Kulkarni et al.[8] Reported that 56.67% were male and 43.33% were female in contrast with Nahla. I. Al-Gabban et al.[9] reported that Hyperbilirubinemia was found in 57% male babies and 43% of female babies.

Prematurity is a well-known risk factor for neonatal hyperbilirubinemia. In the present study 41.88% similar to. Narang et al.[5] inconstant with Kulkarni et al.[8] Amar Shah et al.[10], Bedowra Zabeen et al.[11] reported that preterm babies constituted 73.3% of hyperbilirubinemic babies.

In the present study average gestational age at presentation is 34.96 weeks. Bedowra Zabeen et al.[11] reported the mean gestational age at presentation to be 33.8 weeks. Kulkarni et al[8] Nahla I.[9] reported the mean gestational age at presentation to be 36.12±2.5 weeks.

Causes and Factors Aggravating Neonatal Hyperbilirubinemia: In the present study of the 160 cases, 156 (97.5%) cases were of unconjugated hyperbilirubinemia and 4(2.5%) cases were of persistent conjugated hyperbilirubinemia.

In the present study the incidence of physiological jaundice was 48.76% which was lower than values reported by Anil Narang et al.[5] (57.8%) but it was higher than values reported by Singhal et al.[6] (34.4%) and Kulkarni et al.[8] (35%). Nahla I.[9] In most of the cases of physiological jaundice group more than one risk factor was present.

Septicemia was present in 34(21.25%) cases in the present study. Bedowra Zabeen et al.[11] reported the incidence of septicemia to be 26.7%. But it was higher than other studies, Singhal et al.[6] (5.7%), Anil Narang et al.[5] (7.4%), Kulkarni et al.[8] (8.34%), Amar Shah et al.[10]

(12%), Henny Harry et al.[7] (14%), Choudury Habibur et al.[12] (17.6%). The increased incidence may be due to referral of more sick babies with hyperbilirubinemia to our General Hospital.

ABO incompatibility was present in 27(16.87%) cases in the present study. It is comparable with Kulkarni study.[8] (15%) and Amar Shah Study.[10] (15%) and Singhal et al.[6] study (14.3%). But it was higher than Narang et al.[5] (6.1%), Bedowra Zabeen et al.[11] (13.3%), Nahla I.[9] (9.7%) and Choudury Habibur et al. (11.3%).

Rh incompatibility was present in 10(6.25%) cases. It is comparable with Kulkarni et al.[8] (6.6%), Amar Shah et al.[10] (8%), Singhal et al.[6] (8.1%), Nahla.[9] Of the 10 cases in the present study one was premature baby. 5 cases were given exchange transfusion. 1 case had sibling history of jaundice and it was of mild nature. In our study, as in all other studies the incidence of ABO incompatibility was higher than Rh incompatibility.

Persistent conjugated hyperbilirubinemia accounted for 4(2.5%) cases in the present study. Of these 2 cases were neonatal hepatitis, one case was EHBA, one case was of galactosemia.

Time of detection of clinical jaundice: Mean age of onset of jaundice varied with cause/ aggravating factor. Hemolytic jaundice presented early at 23±7.39 hours (Rh hemolysis), 37±1.73 hours (ABO hemolysis) compared with other causes. Physiological jaundice – 62.8±18.57 hours. Prematurity presented late on 4th day of life (89.5±13.21), septicemia (81.0±26.21), birth asphyxia (66.15±13.37) and birth injuries (60.06± 16.07).

Peak serum bilirubin values achieved due to various causes of hyperbilirubinemia: Peak serum bilirubin values are highest in haemolytic diseases: Rh hemolysis (22.62±2.4mg/dL) followed by ABO hemolysis (20.3±2.6 mg/dL). In these diseases, peak serum bilirubin values were attained earlier than other causes: Rh hemolysis: 49±12 hours and ABO hemolysis: 65±17 hours. Peak serum bilirubin values attained in septicemia are lowest: 15.3±1.9 mg/dL ($p<0.05$). In premature babies age of attainment of peak serum bilirubin level was longer than other causes: 101±12.2 hours. In physiological group, peak serum bilirubin levels attained were 17.1±2.1mg/dL and attained at 92±11.0 hours. Present study values correlate with Singhal et al.[6] study values.

Duration of phototherapy: Mean duration of phototherapy required to bring down serum bilirubin levels to nontoxic levels was longer in hemolytic causes. Rh incompatibility: 115± 5.0 hours. ABO incompatibility: 81±23.0 hours.

Among other causes that required phototherapy, birth injuries were associated with longer duration of phototherapy: 69.6±25.1 hours.

Physiological group required short duration of phototherapy (31.8±7.8 hours). Premature babies required 52.75±22.91 hours. Septicemia required 34.±11.5 hours of phototherapy and birth asphyxia required 65±29.51 hours of phototherapy.

Complications of phototherapy: Out of 160 cases, 153 cases were given phototherapy. Only 6 cases developed complications. They were transient erythema: 3 cases, fever: 1 case, apnoea/ bradycardia: 1case, hypocalcaemia: 1 case.

Exchange transfusion: Double volume exchange transfusion was done in 14 cases. 5 cases were due to Rh haemolysis, 4 cases due to ABO haemolysis, 4 cases in preterm due to exaggerated physiological jaundice and 1 case due to birth injury. In all cases exchange transfusion was done only one time only. All cases recovered uneventfully.

Outcome: In the present study, only 4 cases died of causes unrelated to jaundice. Two were due to extremely low birth weight, 1 case due to septicemia and 1 case due to birth asphyxia. All other cases recovered uneventfully.

SUMMARY: In the present study, physiological jaundice was found to be the common cause. Septicemia, ABO incompatibility, Rh incompatibility were found to be the common causes for pathological jaundice. Prematurity, low birth weight were found to be the major risk factors contributing to neonatal hyperbilirubinemia which are preventable. Early diagnosis of neonatal hyperbilirubinemia and effective management using phototherapy and exchange transfusion according to need improves outcome and prevents development of kern icterus.

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