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Original Research Article

Etiology and clinico-hematological profile of neonates with pathological unconjugated hyperbilirubinemia: a tertiary care centre experience

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ABSTRACT

Background: Jaundice is visible manifestation of raised serum bilirubin. Jaundice in newborns is not an uncommon occurrence. Usually jaundice in newborn is due to elevation of unconjugated bilirubin. There are varied causes of unconjugated hyper bilirubenemia. This study was conceptualized to see the etiology and clinico-hematological profile of neonates with pathological unconjugated hyperbilirubinemia who were admitted in the specific time frame in Sharda Hospital, Greater Noida which is a tertiary care hospital in Western U.P.
Methods: This is a retrospective study in which data of all neonates admitted to NICU with unconjugated hyperbilirubinemia requiring phototherapy and/or exchange transfusion in the period 1.7.2018 to 31.12.2018 was collected and analyzed. History including birth weight, mode of delivery, gestational age, mother's blood group, etc. was recorded. Complete physical examination and investigation done for diagnosis noted.
Results: It was seen that out of 438 admissions in NICU, 63% had neonatal jaundice and 18.8% of this had pathological unconjugated hyper bilirubenemia. 63.5% were males and 36.5% females. Majority were term babies. Most of the babies developed jaundice on day 3 of life. In 61% cases no cause for jaundice could be ascertained despite investigations for the same. ABO and Rh incompatibility accounted for 15.30% and 5.7% cases respectively. All patients received phototherapy and 3.8% underwent exchange transfusion.
Conclusions: From the study it can be concluded that although blood group incompatibility is an important cause of pathological unconjugated hyper bilirubenemia but in most of the cases no cause is usually found.

Keywords: Breast feeding jaundice, Pathological unconjugated hyper bilirubinaemia, Western Uttar Pradesh

INTRODUCTION

Jaundice is visible manifestation of raised serum bilirubin. Jaundice in newborns is not an uncommon occurrence. Usually jaundice in newborn is due to elevation of unconjugated bilirubin. Almost all new-born infants have a serum or plasma total bilirubin (TB) level >1 mg/. Approximately 85% of all term newborns and most preterm infants develop clinical jaundice. Also, 6.1% of well term newborns have a peak TB level >12.9 mg/dl. A TB level >15 mg/dl is found in 3% of normal term infants.[1]

Unconjugated is the most common form of neonatal hyperbilirubinemia. The bilirubin failed to metaboliseandthus cannot be excreted via the normal pathways in the urine and bowel. Unconjugated bilirubin binds with lipids and albumin, and results in the yellow discoloration of the skin and sclera. Though usually harmless unconjugated bilirubin can cross the blood-brain barrier and cause neurotoxic effects.

Hyperbilirubinemias defined as a TB >95th percentile on the hour specific Bhutani nomogram.[1]

Jaundice in newborn has broadly being classified into physiological and non-physiological. If any of the following are present then its non-physiological or pathological.

- Onset of jaundice before 24 hours of age
- An elevation of TB that requires phototherapy
- Rate of rise in total serum bilirubin (TSB) or transcutaneous bilirubin (TcB) level of >0.2 mg/dL/hour
- Associated signs of illness such as vomiting, lethargy, poor feeding, excessive weight loss, apnea, tachypnea, or temperature instability
- Jaundice persisting after 14 days in a term infant.[1]

Physiologic jaundice is due to the normal physiological inability of the newborn infant to process bilirubin adequately because of the combined effects of increased RBC turnover and a transient deficit in bilirubin conjugation in the liver.[2]

This study was conceptualized to see the etiology and clonico-hematological profile of neonates with pathological unconjugated hyperbilirubenemiawho were admitted in the specific time frame in Sharda Hospital, Greater Noida which is a tertiary care hospital in Western U.P.

Objectives of this study to determine etiology and clinico-hematological profile of pathological unconjugated hyperbilirubinemia in neonates admitted in neonatal intensive care unit(NICU), Sharda hospital.

METHODS

In this retrospective study, data of all neonates admitted to NICU with unconjugated hyperbilirubinemia requiringphototherapy and/or exchange transfusion in the period 1.7.2018 to 31.12.2018 was collected and analyzed. History including mothers 'blood group and Rh typing of mother, period of gestation, mode of delivery, predominant feed (mothers milk/other feed) before admission, age at onset of jaundice, gender and birth weight was recorded.

Complete physical examination to find out maturity, cephalohematoma or features of sepsis were noted. Investigations like blood group, Rh typing, total serum bilirubin, direct and indirect bilirubin, direct coombs, reticulocyte count, peripheral blood film, thyroid stimulating hormone(TSH) collected. Sepsis screen and blood culture reports analyzed where clinical features of sepsis were present. Other investigations done like ultrasound abdomen, PT, INR, G6PD, hemoglobin electrophoresis, osmotic fragility test if done to rule other causes of unconjugated hyperbilirubinemia were noted.

Inclusion criteria

All neonates admitted to NICU in Sharda Hospital with unconjugated hyperbilirubinemia requiring phototherapy and/or exchange transfusion in the period 1.7.2018 to31.12.2018.

Exclusion criteria

- Age >28 days
- Direct bilirubin ≥ 2mg/dl or > 15% of total bilirubin
- Patients having major congenital anamolies
- Birth weight <600gms
- Gestational maturity <26week.

RESULTS

A total of 438 patients were admitted in NICU during the study interval 1.7.2018 to 31.12.2018, of which 275 were term and 133 were preterm babies. 276 (63%) out of 438 had neonatal jaundice. 18.8% of patients' with neonatal jaundice had pathological unconjugated hyperbilirubenemia.

Majority of babies were males ,i.e. 33 (63.5%) and 19 (36.5%) females.

In terms of gestational age, out of 52 patients, 30 were term and 22 were preterm babies. The lowest gestational age seen was 26-28 weeks. 2 patients were there. There were 18 patients of gestational maturity between 30-35 completed weeks while 2 patients were between 36 to 37 completed weeks gestation.

Among those affected, majority were born at term. 90% were appropriate for gestational age, 7.60% small for gestational age and 1.90% large for gestational age.

There were 82.80% breast fed, 5.70% were kept nil per oral in view of illness and only 11.50% were top fed.

Majority of patients, 32.60%, developed jaundice on day 3 of life followed closely by day 4 at 28.80% and then day 5 at 15.38%. 3 patients out of 52 (5.7%) presented with jaundice after 2 weeks of age. Similarly only 5.7% was noted to have jaundice on day 2 of life.

As for the cause of jaundice, in 61.5% no cause was found while ABO and Rh incompatibility accounted for 15.30% and 5.70% respectively. Breastfeeding jaundice was seen as third most common cause with 11.50% newborn diagnosed with the same.

Out of 7 patients who had evidence of hemolysis, ABO incompatibility was seen in 4 and Rh incompatibility in 2.

Incidence of sepsis, anaemia and cephalhematoma was found to be 34.60%, 9.60% and 1.90% respectively. All infants tested for hypothyroidism and G6PD deficiency

were negative in the study. All patients received phototherapy and only 2 out of 52, i.e., 3.84% went through exchange transfusion.

Table 1: Distribution of patients (n= 438).

Total NICU admissions	438	
Total term patients	275	
Total preterm patients	133	
Total post term patients	30	
Total patients with neonatal jaundice	276	63.01%
Total patient with pathological unconjugated Hyperbilirubenemia.	52	18.8%
Preterm	22	42.30%
Term	30	57.70%
AGA	47	90.30%
SGA	4	7.60%
LGA	1	1.90%
Breast fed/ebm	43	82.80%
NPO	3	5.70%
Top fed	6	11.50%
Males	33	63.5%
Females	19	36.5%

Table 2: Age wise distribution of time of development of jaundice.

Day 2	3	5.70%
Day 3	17	32.6%
Day 4	15	28.8%
Day 5	8	15.38%
Day 6	4	7.6%
Day 9	2	3.8%
Day 20	1	1.9%
Day 22	1	1.9%
Day 25	1	1.9%

Table 3: Distribution of cause of jaundice and other features (n=52).

ABO incompatibility	8	15.30%
Rh incompatibility	3	5.70%
Breast feeding jaundice	6	11.5%
Breast milk jaundice	3	5.7%
No cause found	32	61.5%
Features of acute bilirubin enceph	1	1.9%
Anaemia	5	9.60%
Sepsis	18	34.60%
Evidence of hemolysis	7	13.46%
Cephalhematoma	1	1.9%

Only 5 mothers out of 52 (9.60%) have not taken any antenatal check ups while 90% mothers were booked cases, equal percentage of primigravida and multigravida mothers, and only one was twin pregnancy. 11.50% mothers had history of abortion. 55.80% were delivered vaginally while 44% had caesarian section. 75% of patients with pathological unconjugated hyper bilirubenemia were born in the Sharda Hospital while 25% were outborn, either home delivery or other institutes.

Table 4: Maternal characteristics (n=52).

Booked	47	90.40%
Unbooked	5	9.60%
Single pregnancy	51	
Twin pregnancy	1	
H/o abortion	6	11.50%
Primi gravida	26	50%
Multi gravida	26	50%
LSCS	23	44.23%
NVD	29	55.80%
Inborn	39	75%
Outborn	13	25%

DISCUSSION

Out of 438 admissions in NICU during 1.7.2018 to 31.12.2018, 276 (63%) patients developed neonatal jaundice. 52 of these i.e, 18.8% patients had non physiological unconjugated hyperbilirubinemia and were included in the study. In other studies incidence was found to be between 5 to 25%.[3-7]

In the present study 63.5% babies were male and 36.5% female. Among out born babies majority were males this could be because of the health seeking behavior of people. Male gender is a known risk factor for pathological jaundice. In a study, 64.2% of those who developed pathological hyperbilirubinemia were males. [4,8]

Out of 52, 55.80% were born by normal vaginal delivery and 44.23% by LSCS. High incidence of jaundice in babies born by normal vaginal delivery could be because rate of NVD was higher. Normal vaginal delivery is known to be associated with a higher chance of neonatal jaundice. This was also found in a study performed in Iran, but the opposite of this was seen in a study in West Bengal.[9,10]

Breastfeeding was associated with neonatal jaundice in some studies, but most of them also linked the breastfeeding with low calorie intake and dehydration.[11-13] In this study about 63.5% babies who developed jaundice were exclusively breast fed and 19.20% were given expressed breast milk only. As those who were given expressed breast milk had other factors influencing hyperbilirubinemia, the association between the two could not be ascertained.

In the present study maximum neonates were found to have jaundice on day 3 of life (32.6%) followed closely by day 4 (28%). Similar trend is seen in other studies.

This is in accordance with the natural progression of physiological jaundice, which usually peaks between days 3 and 5 after birth and then bilirubin levels return to normal by day 10.[12-15]

In this study in 61.5% patients, no cause could be identified. Between 60%–80% of healthy infants are expected to present with idiopathic neonatal jaundice.[16,17]

ABO and Rh incompatibility as cause of jaundice was seen in 15.30% and 5.70% patients respectively.

In a study by Sahoo et al in 2016, incidence for ABO and Rh incompatibility was found to be 16% and 5.7% respectively.[18]

In a study of a population of newborns in Turkey, there was a 14.8% incidence of ABO incompatibility, with 21.3% of these babies exhibiting significant hyperbilirubinemia and 4.4% exhibiting severe ABO hemolytic disease.[19]

In 11.50% babies BF Jaundice was present .Breastfeeding jaundice occurs because of inadequate intake of breast milk by the neonate, either due to inadequate dietary intake by the mother or due to improper breastfeeding techniques. If a baby passing urine adequately i.e., has 4-6 thoroughly wet diapers in a day, passes stools 3-4 times/day by day 4 of life and stool colour has changed to mustard yellow and is mushy in consistency by day 4 then the baby is said to be feeding adequately.[3] A body weight loss of more than 7-10% by day 3 is taken as an objective measure of inadequate breastfeeding. Breastfeeding jaundice, a preventable form of non-physiological jaundice, develops in 13% of exclusively breastfed infants during the 1st week of life.[20-23]

In this study, 3 patients, i.e., 5.7% out of 52 had breast milk jaundice. A diagnosis of breast milk jaundice should be investigated if the serum bilirubin is predominantly unconjugated, other causes of prolonged jaundice have been eliminated and the infant is in good health, vigorous and feeding well and gaining weight adequately. 3 babies who presented after day 20 of life were kept as BM jaundice as no other cause was found. About 2%-4% of exclusively breastfed babies have jaundice in excess of 10 mg/deal in the third week of life. These babies in the third week of life with bilirubin serum levels higher than 10mg/dl should be considered for prolonged jaundice.[16,24,25]

Late-onset human milk jaundice usually occurs from the sixth through the fourteenth day after birth and may persist for 1 to 3 months. A few theories hypothesize the cause of human milk jaundice, but the exact mechanism is not entirely clear. It is believed that human milk contains beta-glucuronidases and no esterified fatty acids that inhibit enzymes that conjugate bilirubin in the liver.[26-28] All infants tested for hypothyroidism and G6PD deficiency were negative in the study.

CONCLUSION

The incidence of pathological unconjugated hyperbilirubinemia in this center is about 18%. Although breast feeding jaundice and ABO incompatibility are important causes, in the majority ,i.e., 61%, no cause for jaundice is found. Anaemia was seen in 9.60% patients. 34.60% patients had sepsis and only 1 patient had features of acute bilirubin encephalopathy.

Out of 7 patients who had evidence of hemolysis, ABO incompatibility was seen in 4 and Rh incompatibility in 2. In 1 patient, probably minor group incompatibility was present as G6PD screen was negative and test for minor groups could not be done.

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Ethical approval: The study was approved by the Institutional Ethics Committee

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