RESEARCH ARTICLE

A STUDY OF NEONATAL HYPERBILIRUBINEMIA IN A TERTIARY CARE HOSPITAL

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ABSTRACT
Background: Neonatal Hyperbilirubinemia is a common problem encountered in neonates and often requires admission and treatment.
Aims & Objectives: To determine the incidence, etiology and risk factors associated with neonatal hyperbilirubinemia in a tertiary care hospital.
Materials and Methods: A retrospective study was conducted on data obtained on live births for 2012 and 2013.All treated cases of neonatal hyperbilirubinemia were analyzed and data on gender, gestation age, mode of delivery, blood group incompatibility, sepsis, parity and birth weight were obtained.
Results: 753 neonates were treated for hyperbilirubinemia, the total number of live births was 5589. The incidence of neonatal hyperbilirubinemia was 13.47%. ABO blood group incompatibility was the most common cause of hyperbilirubinemia.
Conclusion: Blood Group incompatibilities, sepsis, and cephalohematoma were the common causes of hyperbilirubinemia, however in nearly a third of all cases etiology could not be determined. Preterm gestation and low birth weight were associated risk factors.
Key Words: Neonatal Hyperbilirubinemia; Blood Group Incompatibility; Preterm; Low Birth Weight

Introduction

One of the most common reasons for admission of neonates in the Neonatal intensive care unit is indirect or unconjugated hyperbilirubinemia. Jaundice may be noticed in 60% of term babies and 80% of pre-terms.[1] Neonatal jaundice is the occurrence of elevated bilirubin levels in the blood. It may be physiological or pathological. If the concentration of non-conjugated bilirubin in the blood is too high, it breaches the blood brain barrier and bilirubin encephalopathy occurs with serious consequences for the child.[2] The etiology and risk factors for indirect neonatal hyperbilirubinemia is varied and multifactorial. A study done in Australia revealed that the incidence of severe neonatal jaundice was between 7.1 and 45 per 100,000 births and of kernicterus at 0.4-2.7. The causes and risk factors associated were ABO and other blood group incompatibilities, glucose-6-phoshate-dehydrogenase deficiency, infections, prematurity, male gender, ethnicity, breastfeeding and early hospital discharge.[3] Knowing the risk factors and causes would help in devising strategies in managing hyperbilirubinemia and also in counselling parents. The purpose of this study is to estimate the incidence of neonatal hyperbilirubinemia in a tertiary care hospital and to determine the underlying causes and risk factors for neonatal hyperbilirubinemia.

Materials and Methods

This retrospective study was done in a tertiary care teaching hospital. All live births in the hospital in the years 2012 and 2013 were included. Data on neonates treated for unconjugated hyperbilirubinemia in the two year period was collected. The neonates were predominantly treated with phototherapy and a small minority required exchange transfusion. History including gestational age, gender, birth weight, birth order, breast feeding, formula feeding, mode of delivery and family history of jaundice were noted. The physical examination findings revealing the presence of cephalohematoma or suspicion of sepsis was noted. Results of investigations including blood group and Rh type of mother and neonate, serum bilirubin levels, direct coombs test, retic count, peripheral smear, evidence of sepsis from C Reactive Protien, TC/DC, blood culture were collated and considered to determine the etiology and risk factors.

Results

In the present study the total number of live births in 2012 and 2013 were 5589, and 753 neonates were treated for hyperbilirubinemia. This is shown on Table 1.

The incidence of hyperbilirubinemia in our study was 13.47%. ABO incompatibility was the most common cause, in nearly one third the cause was not known, 11.6% of the treated neonates were diagnosed with sepsis. 9.4% had Rh incompatibility and cephalohematoma was present in 4.6%. This is

illustrated in Figure 1.

Among the 753 treated neonates, males slightly outnumbered females, two thirds were term neonates. Low birth weight was observed in 27.7% of neonates, 263 babies were born to multiparous mothers and 490 were delivered by primi mothers. 420 babies were delivered vaginally and 333 babies by caesarean section. The factors associated with hyperbilirubinemia is shown on Table 2.

Table-1: Total Live births and neonates treated for hyperbilirubinemia

Year	Live Births	Neonatal Hyperbilirubinemia
2012	2611	364
2013	2978	389
Total	5589	753

Table-2: Factors associated with unconjugated neonatal hyperbilirubinemia

Factors Associated		Number	Percentage
Gender	Male	403	53.5
	Female	350	46.5
Gestational Age	Term	506	67.1
	Preterm	247	32.9
Birth Weight	Low Birth Weight	105	13.9
	Very Low Birth Weight	70	9.3
	Extremely Low Birth Weight	35	4.6
Parity	Primi	490	65.1
	Multi	263	34.9
Mode of Delivery	Caesarean Section	333	44.2%
	Normal Vaginal Delivery	420	55.8%

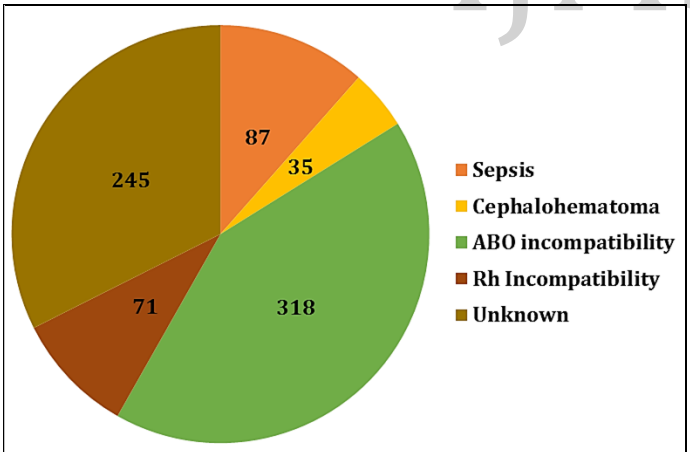

Figure-1: Causes of neonatal hyperbilirubinemia

Discussion

In our study 753 neonates required either phototherapy or exchange transfusion as treatment for unconjugated hyperbilirubinemia. The incidence of hyperbilirubinemia in our study was 13.47%. The most common etiology or risk factor implicated was ABO incompatibility. These observations are similar to the results of other studies. A study done in Kahramanmaraş, Turkey concluded that ABO incompatibility was the most common cause of severe neonatal hyperbilrubinemia.[4] An Iranian study in Fars province revealed that the most common causes of severe indirect hyperbilirubinemia were sepsis, blood group incompatibility, G6PD deficiency, and unknown. Risk factors of severe hyperbilirubinemia were Male sex, previous siblings with severe hyperbilirubinemia, male sex, normal vaginal delivery, and breast feeding.[5] A Croatian study showed that neonatal jaundice was associated with birth weight, maternal infections, gestational age and premature rupture of membranes.[2] More than one risk factor may be present in a neonate, both preterm gestation age and blood group incompatibility may co- exist and contribute in causing hyperbilirubinemia. A review article published in North America suggested that the etiology of neonatal hyperbilirubinemia is multifactorial. Late preterm gestational age, exclusive breastfeeding, glucose-6-phosphate dehydrogenase deficiency, ABO haemolytic disease, East Asian ethnicity and a history of a sibling being treated for hyperbilirubinemia were the most common risk factors associated.[6] The results can show inter regional variation and studies done in different parts of the world have sometimes implicated different risk factors. 18,985 New born infants born in Sarlahi district in Nepal from May 2003 to June 2006 were studied and birth weight, difficulty in feeding, gender, primiparity, oil massage, ambient air temperature, prolonged labour and ethnicity were the major risk factors.[7] An Iranian study investigated the causes of neonatal hyperbilirubinemia requiring blood transfusions, 118 neonates were included in the study and the researchers revealed that the most common causes were ABO incompatibility (38.1%), unknown etiology (25.4%), Rh incompatibility (16.1%), Sepsis(8.5%) and urinary tract infection (5.1%). Vaginal delivery and exclusive breast feeding and male gender were seen more among patients who required exchange transfusion.[8] Some studies have also indicated that neonatal hyperbilirubinemia can result in long-term sequelae. A study in the United States included 54,795 live births and 40,063 of these children were followed up until at least 7 years of age and the study demonstrated that neonatal hyperbilirubinemia was associated with increased risk of childhood asthma.[9] A Taiwanese study evaluated data on 11,328 children and concluded that neonatal jaundice increases the rate and complications of childhood allergic rhinitis.[10] This suggests that children treated for neonatal hyperbilirubinemia may require further childhood follow up. 32.9% or nearly a third of the neonates who required treatment in our study was pre-terms. The risk of hyperbilirubinemia in pre-terms is

well established. Near Term infants (35-37 weeks of gestation) are 2.4 times more likely to develop significant hyperbilirubinemia than term neonates.[11] In the present study in 245 (32.6%) of the neonates, no etiology or risk factor could be attributed as the cause of hyperbilirubinemia. This was similar to the study done in Mashad Iran[8] and in that study unknown etiology accounted for 25.4% of neonatal hyperbilirubinemia cases. A Canadian study revealed that in the majority of neonatal hyperbilirubinemia cases the underlying cause was not identified.[12] However a study in Catania, Italy concluded that in most cases of neonatal hyperbilirubinemia, etiology can usually be well defined.[13] One of the probable causes responsible for hyperbilirubinemia in our study could be glucose-6-phosphate dehydrogenase deficiency, but investigations to confirm this possibility were not done in our study primarily because the requisite investigations are expensive and not affordable by all. A large proportion of the 'unknown causes' in our study might be due to glucose-6-phosphate dehydrogenase deficiency. Mass newborn screening for glucose 6 phosphate dehydrogenase deficiency in Singapore since 1965 resulted in nearly 1.6 million newborns being screened and the incidence of deficiency was 1.62%. Over the last 20 years there have been no reported cases of kernicterus with G6PD deficiency.[14] A study in Isfahan, Iran revealed that the overall incidence of G6PD deficiency in newborns was 3.2%.[15] Race, Gender and ethnicity also influence the risk of neonatal hyperbilirubinemia and its etiology, a study in the U.S. revealed that Neonatal Hyperbilirubinemia and especially resulting from glucose-6-phosphate dehydrogenase deficiency is more common among African American males.[16] A descriptive observational study with longitudinal design done in 109 newborns at the Institute of Postgraduate Medical Education and Research, Kolkata revealed that 14.68% of the newborns were G6PD deficient and 23.8% of them developed severe neonatal hyperbilirubinemia compared to 12.5% of non G6PD deficient who developed severe neonatal hyperbilirubinemia.[17] These studies indicate that G6PD deficiency is one of the more common causes of neonatal hyperbilirubinemia and it is desirable that we increase the gamut of investigations while managing hyperbilirubinemia in neonates. A Turkish study concluded that reticulocyte count, the presence of a sibling with neonatal jaundice and a positive direct antiglobulin test were good predictors for the development of significant hyperbilirubinemia and a serum bilirubin levels of 4 mg/dL and 6 mg/dL at six hours of life are good predictors of severe hyperbilirubinemia.[18] One of the risk factors attributed in other studies was an early discharge, some studies have advocated serum bilirubin screening. A study in Pennsylvania recommended that A pre-discharge total serum bilirubin measured as a universal policy would help in targeted intervention and follow-up in a safe, cost-effective manner.[19] A retrospective cohort study assessed the impact of universal bilirubin screening in 358086 infants with a gestational age of 35 weeks or less and birth weight of less than 2 Kgs and concluded that universal bilirubin screening was associated with a significantly lower incidence of severe hyperbilirubinemia but also with increased phototherapy use.[20] Some doctors and researchers are uneasy with frequent blood sampling and instead endorse transcutaneous bilirubin assessment. A meta - analysis of 22 studies published in 2013 concluded that transcutaneous bilirubin devices are reliable in estimating bilirubin levels in preterm infants and could reduce the frequent need of blood sampling.[21]

Conclusion

The incidence of neonatal hyperbilirubinemia in our study was 13.47% and this indicates that it is a common problem encountered in our Neonatal Intensive Care Units and Hospital. The most common risk factor associated was ABO incompatibility. Nearly a third of the cases had no attributable cause or associated risk factor. Preterm gestation, primi delivery and low birth weight also showed a strong association with neonatal hyperbilirubinemia.

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