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A Study of Haemolytic Disease of the Newborn Secondary to Rheseus Alloimmunisation in a Tertiary Care Hospital

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ABSTRACT

Neonatal Jaundice is the commonest cause of admission for newborns. Rh incompatibility is one of the etiologies responsible for neonatal jaundice. The objectives of the study wereto determine the incidence and associated risk factors for neonatal hyperbilirubinemia resulting from Rh incompatibility in a tertiary care hospital. A retrospective study was done for a 2 year period from January 2012. Data on mothers and babies blood group, direct coombs test, cord blood hemoglobin and bilirubin were analyzed. Gender, parity, birth weight and mode of delivery were also recorded.5589 live births were recorded in 2012 & 2013. There were 208 Rh incompatible deliveries,71 newborns required treatment for unconjugated hyperbilirubinemia. Jaundice was 3.2 times more likely in Rh positive babies born to multiparous Rh negative mothers. The incidence of Rh isoimmunisation resulting in Hyperbilirubinemia was high in our study and was more in multiparous women

Key Words: Neonatal Hyperbilirubinemia, Blood Group Incomaptibility, Rh Alloimmunisation

INTRODUCTION

Hyperbilirubinemia is a common problem encountered in newborn care. Hyperbilirubinemia is the commonest morbidity in the neonatal period and 5-10% of all newborns require intervention for pathological jaundice.^[1] One of the causes of unconjugated neonatal hyperbilirubinemia is Rh incompatibility. Red-cell alloimmunization is the main factor of hemolytic fetal anemia and severe neonatal jaundice, early intravenous injection of 200 to 300 IU or more of Rh immunoglobulin helps in preventing alloimmunization.^[2] Before immunoprophylaxis was available, hemolytic disease of the newborn affected 1% of all newborns and was responsible for the death of one baby in every 2,200 births.^[3] Routine antenatal anti-D prophylaxis reduces the incidence of sensitization and hence of hemolytic disease of the newborn. The economic model suggests that anti-D prophylaxis given to all RhD-negative pregnant women is also very cost-effective.^[4] Deaths attributed to RhDalloimmunisation fell from 46/100,000 births before 1969 to 1.6/100,000 in 1990.^[5] Red blood cell alloimmunization in pregnancy continues to occur despite the widespread use of both antenatal and postpartum Rhesus immune globulin (RhIG), mainly due to inadvertent omissions in administration as well as antenatal sensitization prior to RhIG given at 28 weeks' gestation.^[6] The purpose of the study is to estimate the incidence of rhesus disease of the newborn in a tertiary care hospital and also to determine the associated risk factors.

MATERIAL AND METHODS

This Retrospective observational descriptive study was done in a tertiary care hospital on deliveries conducted between January 2012 and December 2013. The total number of live births during this period was recorded and data on treated cases of unconjugated hyperbilirubinemia in neonates was collected. The neonates were all treated either by using phototherapy or exchange transfusion. Using a proforma, details on diagnosis at discharge, mothers and newborns blood group, direct coombs test, mode of delivery, parity, gender, cord bilirubin and hemoglobin levels were noted. The birth weight and physical examination findings of the presence of cephalohematoma or any indication of sepsis were collated. Results of other relevant investigations such as peripheral smear, retic count, blood culture, C reactive protein and total and differential counts were also recorded. After the etiology was determined the hyperbilirubinemia cases were further segregated to hyperbilirubinemia attributed to Rh incompatibility and others. The Rh incompatibility cases were further analyzed to determine the associated risk factors.

RESULTS

In the present study there were 5589 live births, 3.7% of those deliveries occurred in mothers who were Rh-ve and their newborns Rh+ve . In 34.1% of the Rh incompatible deliveries, the neonates required treatment for hyperbilirubinemia. Among all the neonates treated for unconjugated hyperbilirubinemia ABO incompatibility was the most common cause and constituted 42.3% of the

newborns treated. In 32.5% the etiology could not be determined, in 11.5% of the cases sepsis was implicated, cephalohematomas were present in 4.6% and in 9.4% Rh incompatibility was attributed as the cause. Table 1 shows the total live births and the number of neonates treated for unconjugated hyperbilirubinemia during the study period.

Caesarean section was the mode of delivery in 35% of Rh incompatible deliveries, 62% of the deliveries occurred in multiparous women and 38% in primi mothers. 14.2% of the newborns delivered to primisrequired treatment forhyperbilirubinemia whereas in the case of multiparous the incidence was 45.8%, therefore treatment forhyperbilirubinemia was 3.2 times more likely in Rh+ve babies born toRh-ve

multiparous women. Male newborns accounted for 57% and females 43%. Twenty one percent of the babies had a low birth weight. Table 2 shows the factors associated with Rh incompatibility.

Among the Rh negative mothers, 45% had O blood group, 26% had A, 22% had B and 7% AB blood group. Figure 1 shows these statistics in terms of numbers and proportions.

Among the Rh positive newborns, 36% had O blood group, 28% had A, 27% had B and 9% had AB blood group. These are displayed in terms of numbers and proportions in Figure 2.

In 7 newborns the direct coombs test was positive and among them, 6 newborns had cord blood bilirubin exceeding 4.5mg% and cord hemoglobin exceeding 11 gm%. All these neonates were born to multiparous mothers.

Table1: Total live births and treated neonatal hyperbilirubinemia numbers 2012 & 2013

Total Live Births 2012 & 2013	5589
Rh incompatible deliveries 2012 & 2013	208
Total cases treated for Neonatal Hyperbilirubinemia 2012 &2013	753
Treated cases of Neonatal Hyperbilirubinemia due to Rh incompatibility 2012 & 2013	71

Table 2: Associated factors in Rh+ve neonates born to Rh-ve mothers.

Mode of Delivery		
1	Normal Vaginal Delivery	131
2	Caesarean Section	77
Parity		
1	Multiparous	131

2	Primi	77
Gender		
1	Male	119
2	Female	89
Birth Weight		
1	Birth Weight > 2500 gms	44

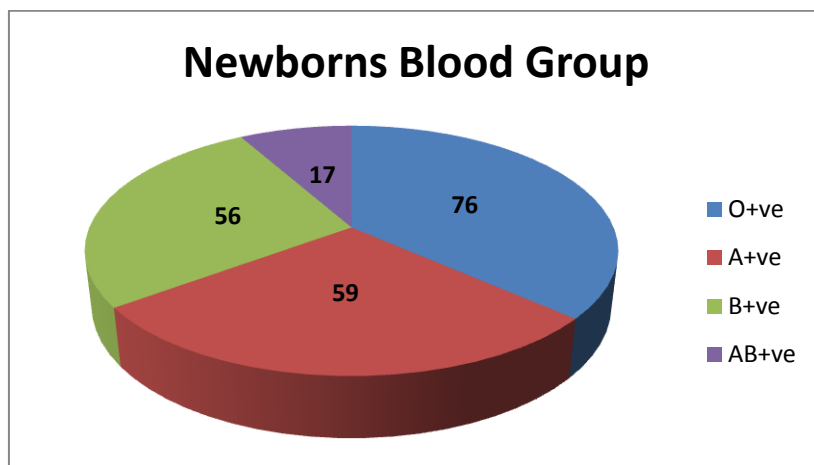


Figure 1: Mothers blood group in Rh incompatible cases

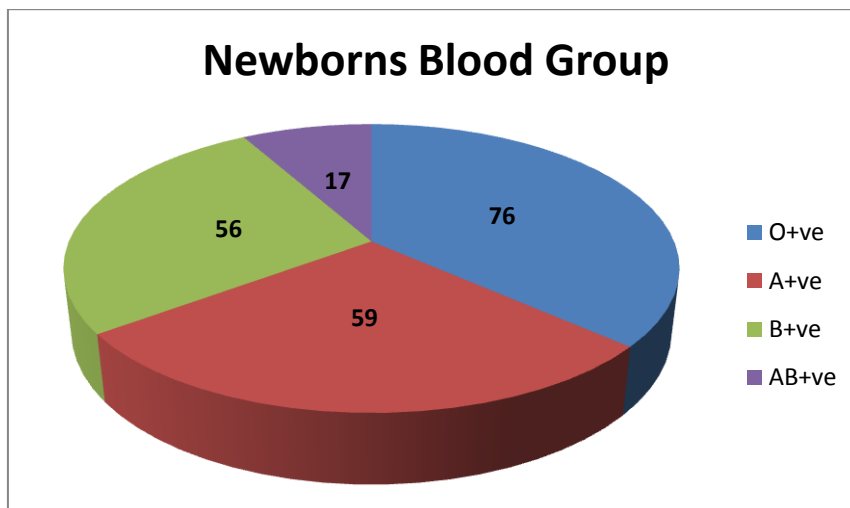


Figure 2: Babies blood group in Rh incompatible cases.

DISCUSSION

In the present study, nearly a third of the Rh positive babies delivered to Rh Negative mothers required treatment for hyperbilirubinemia. The status of anti-D prophylaxis in all the mothers could not be determined but a vast majority did receive anti-D prophylaxis. The incidence of Rh-ve blood group in India is 5-10%.^[7] Universal access to Rh immunoprophylaxis, coordinated perinatal-neonatal care, and effective phototherapy has virtually eliminated the risk of kernicterus in many countries.^[8] Despite anti-D prophylaxis alloimmunization can occur. Residual alloimmunization occurs mainly for two reasons: i) failure to administer sufficient anti-D at the correct time after known at-risk events, either during pregnancy or at delivery; and ii) alloimmunization during pregnancy as a result of 'silent' fetomaternal hemorrhage.^[9] There are some small drawbacks with anti-D prophylaxis. Researchers in Australia concluded that Rh D prophylaxis has increased positive direct anti-globulin test results which result in an increase in the number of unnecessary bilirubin measurements.^[10] A study estimated the incidence of RhD immunisation after implementation of first trimester non-invasive fetal RHD screening to select only RhD negative women carrying RHD positive fetuses and concluded that using first trimester non-invasive antenatal screening for fetal RHD to target routine antenatal anti-D prophylaxis selectively to RhD negative women with RHD positive fetuses significantly reduces the incidence of new RhD immunization.^[11] The incidence of Rh isoimmunization varies in

different studies. Current data suggest that the risk of Rh isoimmunization when immunoprophylaxis is not administered is 16% if Rh-positive fetuses are ABO compatible with their Rh-negative mothers.^[12] The incidence of Rh isoimmunization was 17.6% in a study done in Southern India.^[13] In high income countries rhesus immune globulin has reduced the prevalence of hemolytic disease of the newborn secondary to rhesus alloimmunization and only approximately six cases occur in every 1000 live births.^[14] The incidence in our study was a relatively higher 12.7 per 1000 live births. A systemic Cochrane review revealed that the risk of RhD alloimmunisation during or immediately after a first pregnancy is about 1.5%. Administration of 100ug (500IU) anti-D at 28 weeks and 34 weeks gestation to women in their first pregnancy can reduce this risk to about 0.2%.^[15] In 2010, an estimated 373,300 babies were affected with Rh hemolytic disease worldwide. The global estimated prevalence for Rh disease was 276/100,000 live births.^[16] This figure translates to approximately 3 per 1000 live births which is significantly lower than the incidence in our study. A study in Sheffield investigated the cost effectiveness of routine antenatal anti-D prophylaxis in the prevention of hemolytic disease of the newborn and concluded that routine antenatal anti-D prophylaxis provides a cost effective intervention for preventing hemolytic disease of the newborn in the pregnancies of women who are RhD-negative.^[17] A retrospective study done in Christchurch, New Zealand examined 54 sensitizations in 4624 at risk patients recognized

a sensitizing event including previous deliveries in 86.6% of the sensitizations, 46.1% had anti-D prophylaxis per local guidelines, in 12.8%, prophylaxis was given though it did not conform, entirely, to guideline. No prophylaxis at all was given to 41% despite a sensitizing event being recognized.^[18] Researchers in Stockholm conducted a retrospective study on all RhD immunized pregnant women 1990-2008 before the introduction of routine antenatal anti-D prophylaxis and concluded that at least half of the cases could potentially have been avoided by routine antenatal anti-D prophylaxis in the beginning of the third trimester.^[19] Unfortunately in our study, data on anti-D prophylaxis in all cases was not available and therefore we could not include statistics on prophylaxis and its consequences. A British study revealed that 90% and 81-87% of eligible women at 28 and 34 weeks of gestation received antenatal anti-D prophylaxis and the sensitization rate was 0.4%.^[20] A study conducted at John Radcliffe Hospital, Oxford concluded that restricted routine antenatal prophylaxis (first pregnancy only) provides continuing protection for subsequent pregnancies although the mechanism for this is unclear.^[21] 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.^[22] In our study there were seven positive direct coombs test

and six of those neonates had high cord haemoglobin and bilirubin.

CONCLUSION

The incidence of hemolytic disease of the newborn secondary to rhesus alloimmunization was 12.7 per 1000 live births in the present study which was relatively higher than the incidence in other studies. The status of anti D prophylaxis in Rh negative mothers could not be determined in all mothers. Nearly a third of the Rh positive neonates in the study required treatment for hyperbilirubinemia. The occurrence of hyperbilirubinemia requiring treatment was 3.2 times more likely in neonates born to multiparous Rh negative mothers.

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