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Original research article

Study of Hemolytic Disease After ABO Incompatibility in Newborn in Tertiary Care Centre

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Abstract

Background: Better understanding of the clinical characteristics of Hemolytic Disease of the Newborn due to ABO incompatibility helps to optimise care. ABO incompatibility is complex because anti-A and anti-B antibodies are composed mainly of Immunoglobulin M.

Material and methods: This is cross sectional study conducted in theneonatal unit of narayan medical college and Hospital Jamuhar Sasaram Rohtas. A total of 50 neonates with blood group A or B born to mothers with blood group O; with jaundice and or anemia were enrolled during the Study period of two years, The various maternal and neonatal parametersand their association with development of jaundice and or anemia was studied.

Conclusion: Early identification of high risk neonates with ABO Incompatibility, diagnosis and early intervention can reduce morbidity and mortality.

Keywords: Hemolytic Disease of the newborn, Direct Coombs Test, Phototherapy.

Introduction

Hemolytic disease of the newborn due to ABO Incompatibility occurs exclusively in newborns of blood group A or B having mothers of group O. Even though hemolytic disease of the newborn has been reported in a baby whose mother was group A with a high titres of anti B.[1] Jaundice in hemolytic disease of the newborn is more frequent and severe in ABO incompatible black than white newborns and, furthermore, jaundice due to any other cause, is more likely to be moresevere in ABO incompatible babies than compatible ones.[2] The etiology of hemolyticdisease of the newborn due to ABO incompatibility is complex because anti-A and anti-B antibodies are composed mainly of Immunoglobulin M. Since only Immunoglobulin G antibodies cross the placenta, those pregnant women with high levels of Immunoglobulin G anti-A or B with an ABO incompatible fetus will be the ones to give birth to a newborn with ABO hemolytic disease of the newborn.[3] Although hemolytic disease of the newborn as a result of ABO incompatibilityis clinically milder than Rhesus incompatibility, severe hemolysis occasionally occurs, such that some cases require exchange transfusion.[4] It has been noted that hemolytic disease of the newborn due to ABO incompatibility frequently occurs during the first pregnancy, and about 50% of infants are affected unlike Rhesus hemolytic disease of the newborn in which the first born- babies are usually spared orfree of the disease and subsequent babies are the ones that are affected. ABO incompatibility is present in about 12% of pregnancies, with

evidence of fetalsensitization in 3% live births. Less than 1% of births which are ABO incompatible are associated with significant haemolysis. The diagnosis of Hemolytic disease of the newborn due to ABO incompatibility cannot be made serologically using one single test; however several tests together make the diagnosis more probable. In contrast to Rhesus hemolytic disease, the immunological findings in hemolytic disease of the newborn due to ABOincompatibility do not correlate well with the severity of the clinical course.[7] Sometimes it is impossible to differentiate between hemolytic disease of the newborndue to ABO incompatibility and non-antibody mediated hyperbilirubinemia. Hemolytic disease of the newborn can be managed by using any ofthe following modalities; phototherapy, exchange transfusion or intravenous immunoglobulins. Early application of any of these methods in the treatment of hemolytic disease of the newborn prevents bilirubin encephalopathy and kernicterus with subsequent development of severe neurological sequelae or death. Nearly 50% of babies with hemolytic disease of the newborn due to ABO incompatibility do not require treatment. Of the remaining 50%, half of them become extremely jaundiced and without treatment, 90% of them will die and 10% become severely affected by kernicterus. The other half are severely affected in utero and become hydropic. Hemolytic disease of the newborn due to Rhesus incompatibility is preventable and preventable measures are in place in many countries. In contrast thereare currently no preventable measures for Hemolytic disease of the newborn due to ABO incompatibility.[9] ABO incompatibility hence is now the single most common cause of neonatal jaundice.

Objectives

The clinical manifestations of HDN due to ABO Incompatibility.

Review of Literature

Hemolytic Disease of Newborn (HDN) also called Icterus gravis Neonatorumwas first described by **Morgagni** in 1761.ABO blood group system was credited to have been discovered by the Austrianscientist Karl Landsteiner in 1900 AD. He originally described the O blood type as type "C", and in parts of Europe it is rendered as "0" (zero), signifying the lack of Aor B antigen. He was awarded the Nobel Prize in Physiology or Medicine in 1930 forhis work. In 1902, Alfred von Decastello and Adriano Sturli discovered the fourth type,AB. At present, the International Society of Blood Transfusion (ISBT) approves 29 human blood group systems. Zuelzer and Cohen also pointed out the importance of ABO incompatibility asa contributing factor to neonatal jaundice. and Robinson *et al.* associated hyperbilirubinemia to ABO incompatibility. Hemolytic disease of the newborn is a clinical condition in which fetal red blood cells are destroyed by maternal allo-antibodies directed against red blood cell antigens acquired from the father. Immunoglobulin G (Ig G) antibodies that have beenproduced by the mother pass through the placenta and attack the red blood cells of thebaby in circulation. HDN due to ABO incompatibility results from the action of maternal anti A oranti B antibodies on fetal erythrocytes of the corresponding blood group. Hemolysisassociated with ABO incompatibility is similar to Rh hemolytic disease in that maternal anti A or anti B antibodies enter the fetal circulation and react with A or B antigens on the erythrocyte surface. In type A and B individuals, naturally occurring anti B and anti A isoantibodies largely are Ig M molecules that do not cross placenta.[3]In contrast, the allo antibodies present in type O individuals are predominantly Ig G molecules. For this reason ABO incompatibility is largely restricted to type O motherswith type A or B fetus. infants with indirect hyperbilirubinemia were taken as subjects and were compared with a control group of healthy infants. Patients were divided into twogroups. Patients with indirect bilirubin less than 12 mg/dl and having mild disease were classified into Group A and patients having indirect bilirubin more than 12 mg/dl were labeled

as Group B. Out of the 50 patients studied, 23 belonged to group A and remaining 27 to group B. Group C (control group) comprised of50 healthy infants. ABO incompatibility was the leading cause of hemolysis (in 48%)followed by Rh incompatibility (in 22%), septicemia in 26% and G6PD deficiency in 4%. In a prospective study of Clinical Course and Prognosis of Hemolytic Jaundice in Neonates in North East of Iran by Hassan Boskabadi et al., 2011, concluded that Jaundice due to hemolysis was associated with a higher serum bilirubin and more complications like kernicterus. ABO incompatibility was the most common reason forhemolytic jaundice among neonates in north east of Iran. In this study, significant differences were observed between two groups of hemolytic and idiopathic jaundicefor total serum bilirubin, hematocrit, appearance of jaundice, age of admission, duration of hospitalization and incidence of kernicterus ($p<0.001$). Newborns with ABO incompatibility (17%), Rh disease (7%), G6PD deficiency (6%) and minor blood group immunization (2%) developed hyperbilirubinemia. A retrospective cohort study by Preethi et al, in 2011, concluded that mean cord bilirubin was increased in infants with group A and group B born to group O mothers. Significant jaundice was more often seen when mother-infant pair had O andA combination. When significant jaundice was going to develop, serum bilirubin at 12 hours was quite high and it kept on increasing and all the cases in the study grouphad developed significant jaundice by 24 hours. A study by Kalpan M et al, in 2010, on Hemolysis and hyperbilirubinemia inantiglobulin positive, direct ABO blood group heterospecific neonates concluded increased risk of hemolysis and jaundice in O-B Incompatibility. In that study of 164 neonates, 111 were O-A and 53 O-B. Hyperbilirubinemia developed in 85 neonates (51.8%), and tended to be more prevalent in the O-B neonates than O-A neonates (62.3% versus 46.8%; P=.053).

Material and methods:

This is cross sectional study conducted in theneonatal unit of Narayan medical college and Hospital Jamuhar Sasaram Rohtas, Bihar. A total of 50 neonates with blood group A or B born to mothers with blood group O; with jaundice and or anemia were enrolled during the Study period of two years, The various maternal and neonatal parametersand their associ Primary source of information was by observational method on a sample size of 50 term neonates admitted to NICU with neonatal jaundice and or anemia due to ABO Incompatibility. ation with development of jaundice and or anemia was studied. Informed consent regarding participation in the study was obtained in the regional language Data was collected as per the proforma. Questionnaire method, maternal case file and examination of the newborn were used to obtain the required data.

Maternal variables like history of jaundice, first trimester bleeding, gestationalhypertension, mode of delivery and use of drugs during pregnancy were collected. Medication during labour, details of delivery, APGAR score and maternal blood group were collected from the maternal file.

Babies were clinically assessed for age, sex, gestational age, birth weight, previous history of jaundice in the family, day of onset of jaundice, pattern of feeding, fever and other neurological symptoms.

Inclusion Criteria

Term babies admitted to NICU with Neonatal jaundice and or Anemia due to ABO Incompatibility.

Exclusion Criteria

The neonates with history of Birth asphyxia, Sepsis, The neonate with congenital anomalies. Neonate with other known causes of jaundice and hemolysis.
The maternal factors like parity, gestational hypertension, mode of delivery, medication with oxytocin and initiation of breast feeding within 30 minutes and neonatal factors like sex, weight, blood group were considered. The association between these parameters and development of jaundice and or anemia in ABO Incompatibility were studied and the results were compared with other studies.

Results

In this cross sectional hospital based study of 50 newborns with HDN due to ABO incompatibility, the following observations were made. The study results wereanalyzed using appropriate statistical methods.

Table 1: Sex wise distribution of neonates (n=50)

Sex	Number of cases	Percentage
Male	24	48
Female	26	52
Total	50	100

Table 2: distribution of the neonates based on birth weight

Birth weight	Number of cases	Percentage
AGA	42	84
SGA	8	16
Total	50	100

study, 42(84%) of newborns were AGA and 8(16%) were SGA.The mean birth weight was 2.80±0.37 kilograms.
Twenty-nine babies were born through vaginal delivery and 21 were born through LSCS due to various indications like previous LSCS, Deep Transverse Arrest, Cephalo Pelvic Disproportion and failed induction.

Association between the mode of delivery and serum bilirubin level.

There was no significant association (p value 0.36) between the serum bilirubin

Table 3: Distribution of blood group.

Blood group	Number of cases	Percentage
O-A	19	38
O-B	31	62
Total	50	100

O-A and O-B Incompatibility were 19(38%) and 31(62%) respectively.
Three (6%) neonates developed jaundice within first 24 hours of life followedby 13 (26%) on second day, 19 (38%) on third day followed by 15 (30%) on fourth day. Majority of neonates presented with jaundice on third day (38%) followed by fourth day (30%), followed by second day (26%) followed by first day (6%).Mean age of presentation with jaundice was 2.9 ± 0.89 with the range from0 to 4 days.

Table 4:

Hb%	Number of cases	Percentage

<13	9	18.0
>13	41	82.0
Total	50	100.0

Nine (18%) neonates had anemia.
The mean initial hemoglobin was 14.3±2.31 with the range from 9.10 to23.20 g/dl and with microcytic hypochromic blood picture with MCV value < 95. Themean MCV value was 95±5. The mean Reticulocyte count was 16.6 ± 5.3. The meanhematocrit value was 43.6 ± 6.48. The mean platelet count was 1.5 lakh ± 0.3lakh and9 (18%) neonates had thrombocytopenia. There was no significant difference in clinical presentation with respect to various demographic characters like Birth weight, Gender, Day hospitalization, Initial hemoglobin, Initial indirect bilirubin, Positive direct Coombs test, Anemia, Presence of hemolysis, Jaundice within first 24 hours, Duration of phototherapy and number of exchange transfusion, eventhough O-B incompatibility were more in the study group. Mean age of clinical presentation was 2.9 ± 0.89 days. The main clinical manifestation was jaundice and was treated with phototherapy in 98% of the cases.

Discussion

This clinical study on Hemolytic disease of newborn due to ABO Incompatibility was conducted over a period of two years, to study the clinical manifestations and outcome of treatment modalities. Theobservations thus made were discussed in comparison with that of other similar studies. various parameters and their association with the clinical manifestation of ABO Incompatibility were analysed. Neonatal jaundice was the main clinical feature in majority of the cases and mild anemia in few cases. Maternal factors like parity, gestational hypertension, mode of delivery, medication with oxytocin and initiation of breast feeding within 30 minutes and fetal factors like sex,weight, blood group were considered. Awasthi et al observed no significant correlation between the time of initiation of breast feeding and jaundice with p value 0.9.Thus, in the present study, maternal factors like parity, gestational hypertension, mode of delivery, medication with oxytocin and initiation of breast feeding within 30 minutes and neonatal factors like sex, weight, blood group had nosignificant association with development of jaundice and or anemia due to ABO incompatibility, which were the main clinical manifestations. These observations were similar to that of in studies by Ashutosh Kumar et al, Sinem Akgul et al and Kalakheti et al. Sinem Akgul et al (2013), in a retrospective evaluation of 254 newborns withABO incompatibility reported that gender, race, birth weight, and blood type of the infant had no significant relationship with clinical outcome. there was no significant difference in severity and outcome in both O-A and O-B incompatibility, although O-B incompatibility was more. Similar observation was made by Ashutosh Kumar et al, Ella E et al, Sinem Akgul and Bhat YR et al. McDonell et al and Stiller et al concluded that ABO Incompatibility mightcause more fetal anemia in patient with type B blood group. Adewuyi et al observed that anti-B antibodies showed greater hemolytic activity than anti-A antibodies. Sinem Akgu et al, concluded that blood type had no effect on the severity of the hemolytic jaundice due to ABO incompatibility. Mean age of presentation with jaundice was 2.92±0.89 (0-4) days. Mean initial IB was 21.26±3.97 with the range from 12.3 to 31 mg/dl. Three neonates (6%) developed jaundice in the first 24 hours of life followed by 13(26%) on second day, 19 (38%) on third day followed by 15 (30%) on fourth day,hence majority of neonates presented with jaundice on third day (38%) followed by fourth day (30%), followed by second day (26%) and 9 infants (18%) had anemia inthe first complete blood count examination. Mean initial hemoglobin was 14.3±2.31(9.10-23.20) g/dl. Nine (18%) developed anemia. Twenty-two neonates (44%)

had hemolytic findings (microspherocytosis) on peripheral blood smear and 4 neonates (8%) had positive Coombs test. In a study by Akgul (2013), Mean age on the day of admission to hospital was4.4±2.4 (0-9) days. Mean initial IB was 19.9±5.7 (7.1-41.3) mg/dl. Fifteen neonates (9.0%) developed jaundice in the first 24 hours of life and 17 neonates (10.2%) had anemia in the first complete blood count examination. Mean initial hemoglobin was 15.6±2.3 (8.2-20.8) g/dl. Twenty-four neonates (14.5%) had hemolytic findings on peripheral blood smear, and 17 neonates (10.2%) had positive Coombs test.
The direct antiglobulin test should be at least weakly positive for anti-A or anti-B; however, because of the sparse distribution of antigenic sites on a newborn'sRBCs, HDN due to ABO incompatibility may be present even without a positive result on the direct antiglobulin test. A positive Coombs test in ABO incompatible infants does not necessarily indicate disease. Ashutosh Kumar et al (2013) observed p-value of <0.001 and a high predictivevalue of Antiglobulin test for occurrence of disease but for neonates affected by disease, p-value was >0.1 and was statistically insignificant. Thus Direct Antiglobulintest was nonspecific in predicting severity of disease. In Bhat YR et al study (2012), phototherapy was required in46% of the casesand none required exchange transfusion. In Akgul et al study, 10.8% required exchange transfusion and 10.8% required IVIg therapy. identification of high risk neonates with ABO incompatibility might reduce the morbidity and mortality due jaundice and or anemia.

Conclusion

maternal factors like parity, gestational hypertension, mode of delivery, medication with oxytocin and initiation of breast feeding within 30 minutesand neonatal factors like sex, weight, blood group had no significant association withdevelopment of jaundice and or anemia due to ABO Incompatibility.Comparison of neonates with blood group A with B groups showed similar demographic parameters such as birth weight, gender and day of admission.

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