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STUDY OF CORRELATION OF ABO AND RH INCOMPATIBILITY WITH RISK OF NEONATAL HYPERBILIRUBINEMIA IN A TERTIARY CARE HOSPITAL

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ABSTRACT **Background:** Hyperbilirubinemia in a neonate is one of the most common problems that may occur in 60-70 % of term and 80% of preterm babies. It is known to be associated with significant morbidity like neonatal bilirubin encephalopathy and even death. Clinically, and almost exclusively ABO incompatibility occurs in 'A' and 'B' blood group babies of O '+ve' mothers. These babies are reported to be at high risk of severe hyperbilirubinemia. So early intervention, at proper time, is mandatory to prevent these sequelae **Methods:** The aim is to determine the frequency of ABO and Rh blood group incompatibilities and associated incidence of hyperbilirubinemia for the purpose of instituting intervention for better neonatal outcomes. It was a descriptive cross-sectional study that includes 102 neonates born to mother with O or Rh-negative blood group admitted in the post-natal ward for routine newborn care. Serum bilirubin was documented in icteric neonates. **Results:** The incidence of ABO incompatibility in our study was 33.33% and of Rh incompatibility was 4.9%. In ABO and Rh incompatibility group, 41.17% and 20% new born respectively developed clinical jaundice. In ABO incompatibility group, majority, 64.28% did not require treatment, whereas in Rh incompatibility group 100% required treatment. In both ABO and Rh incompatibility exchange transfusion was not required. In ABO and Rh incompatibility, all new-born treated well and no kernicterus was seen. **Conclusions:** In ABO incompatibility, if jaundice develops, it remains in physiological limits. In presence of some aggravating conditions may present as pathological jaundice. It results in significant morbidity but no mortality, so prevention of aggravating factors is very important, in case of ABO and Rh incompatibility.

KEYWORDS : ABO incompatibility, Rh incompatibility, jaundice, neonatal hyperbilirubinemia.

INTRODUCTION

Neonatal period represents the most crucial period for a child's survival.(1) wherein, the neonates are at risk of acquiring many problems. Among these, the major health problems are jaundice, infections, nutritional deficiency, trauma and regulation of body temperature. Of these, jaundice is first affliction that clinically appears, besides thermo regulation disturbances. Physiological jaundice normally occurs between second and fourth day of life, appears in 50% of all full-term new-born. A bilirubin level, exceeding 12 mg/dl for the full-term infant is suggestive of more than normal physiology and should be considered pathological hyperbilirubinemia, can become a worrisome problem, as higher bilirubin levels can cause complication, known as Kernicterus which is associated with neurological abnormalities, hearing loss, motor abnormalities.(2)

Blood group incompatibilities (e.g., ABO, Rh), may increase bilirubin production through increased hemolysis, and it is the most common cause of hemolytic disease of newborn (HDN). The major clinical issue with HDN due to ABO incompatibility is jaundice. ABO incompatibility occurs most frequently but rarely causes severe haemolytic disease of newborn (HDN), while the highly immunogenic Rh D antigen can cause immune response with severe HDN (3,4,5). During this study, we try to establish a relation between ABO and Rh incompability with hyperbilirubinemia. The objectives of the study are -To assess the incidence and severity of ABO and Rh incompatibility in neonatal hyperbilirubinemia and to determine the frequency of ABO and Rh blood group incompatibility among neonates and their mothers with a view on raising awareness on the knowledge of blood groups, screening, and prophylaxis against isoimmunization in pregnancy, thereby improving the outcome of hemolytic disease of the fetus and newborn with its attendant complications.

METHODS

This study was conducted at Dr. D Y Patil Medical Collage and Hospital from June 2020 to November 2020. It was a cross-sectional study that includes all neonates admitted in the postnatal ward born to mothers with O blood group and Rh–ve blood group. Neonates with cephalhematomas, bleeding tendencies, birth asphyxia were excluded from the study. Ethical approval was obtained from the Ethics Committee of the participating institutions, while written informed consent was obtained from the parents or guardians of the neonates. The neonates were examined, Birth weight notes and blood sample was collected for ABO and Rh blood group, serum Bilirubin level was documented for neonates who developed clinical icterus. Treatment given to baby to treat hyperbilirubinemia was recorded. Data obtained were analyzed.

RESULTS

Out of the 102-neonate included in study 41 (40.19%) were male and 61 (59.80%) were female, out of which 31.17% male and 34.44 %female had ABO incompability and 4.8% male and 4.9%female had Rh incompability (Table 1); the incidence of hyperbilirubinemia was 14.63 % in male and 14.75% female in each group. No relation between sex and NNH in ABO and Rh incompatible group (p-value 0.839) was seen.

Table 1: Sex wise ABO And Rh incompability in neonates

SEX	Total	ABO In Compability	Rh incompability
Male	41 (40.19%)	13 (31.17%)	2 (4.8%)
Female	61 (59.80%)	21 (34.44%)	3 (4.9%)

X^2-value = 0.041; p-value = 0.839

Out of 102 patients, 34(33.3%) had ABO Incompatibility and 5 (4.9%) had Rh Incompatibility (Table 2). In which blood group O mothers had 20 (58.82%) neonates with blood group B while 14 (41.17%) mothers had neonates with blood group A. In ABO incompatibility group, 41.1% baby developed hyperbilirubinemia, In Rh incompatibility group, 20% baby developed hyperbilirubinemia (Table 3). Thus, proving ABO incompability is a major risk factor for developing NNH in neonates in this study.

Table 2: Incidence of ABO AND RH incompability

Total Patients	102
ABO incompability	34(33.33%)
RH incompability	5(4.9%)

Table 3: Type of incompability with Hyperbilirubinemia and phototherapy given.

Type Of Incompability	Hyper Bilirubinemia	Phototherapy Given
ABO incompability	14 (41.1%)	5 (35.57%)
Rh incompability	1 (20%)	1 (100%)

In present study 34 (33.33%) mother were primi and 68 (66.66%) mother had multi parity, out of which 8(23.5 %) neonates born to primi mother and 10 (29.4%) neonate born to multi para mother developed NNH and no significant correlation (p value 0.362) was established between parity and NNH. (Table 4)

Table 4: Parity Of Mother And Hyperbilirubinemia

PARITY	Number	NNH
Primi	34(33.33%)	8(23.5%)
Multi	68(66.66%)	10(29.4%)

X^2-value = 0.830; p-value = 0.362

The mode of delivery for mother was 33(32.35%) SVD , 3 (2.94%)Instrumental assisted vaginal delivery and 66(64.70%) LSCS out of which 2(6.06%),1(33.33%)and 12(18.18%) developed NNH respectively(Table 5) which is statistically (p value 0.276) not significant to establish a correlation.

Table 5: Mode Of Delivery And Associated Hyperbilirubinemia

Mode Of Delivery	Number	Hyperbilirubinemia
SVD	33(32.35%)	2(6.06%)
Instrument assisted vaginal delivery	3(2.94%)	1(33.33%)
LSCS	66(64.70%)	12(18.18%)

X^2-value = 2.571; p-value = 0.276

Treatment: Hyperbilirubinemia due to ABO incompatibility, resolved naturally in most cases 9 (64.28%), as there is very mild hemolysis. 5 (35.57%) neonates required treatment, most of them were cured only by phototherapy; 1 (100%) neonate with hyperbilirubinemia with Rh incompability and required phototherapy treatment. (Table 3). In this study hyperbilirubinemia due to ABO and Rh incompatibility, resolves with simple treatment. No neonate developed kernicterus. No neonatal mortality occurred in present study.

DISCUSSION

Most newborns have physiological jaundice. It is most noticeable when the baby is 2 to 4 days old. Most of the time, it does not cause problems, and fades away within 2 weeks. Neonatal physiologic jaundice results from, simultaneous occurrence of the following two phenomena (6)

(1)Bilirubin production is elevated, because of shortened lifespan of fetal erythrocytes, and the higher erythrocyte mass in neonates (7,8). Life span of circulating RBCs in neonates is significantly shorter (80 to 90 days), than adult RBCs (120 days).(9) Fetus has more RBCs than adult (7 million/mm3 compared to adult value of 5 million/mm3).

(2) Low hepatic excretory capacity, because of low concentrations of ligandin, and, low activity of glucuronyl transferase, the enzyme responsible for binding of bilirubin to glucuronic acid (conjugation). Pathologic neonatal jaundice occurs, when additional factors accompany the basic mechanisms. e.g., immune or non-immune hemolytic anemia, polycythemia, and the presence of bruising or extravasation of blood.

ABO incompatibility is the most commonly reported serologic cause of neonatal jaundice but clinically mild as a cause of hemolytic disease of the newborn (HDN) with hyperbilirubinemia than the Rh incompatibility (10,11). Rh negative blood group is present in only 15% of population. It could also be attributed to the fact that Rh incompatibility which was once an extremely common cause of severe hemolysis has now been reduced by the prophylactic administration of anti-D globulin to Rh-negative mothers (11) Frequency of ABO incompatibilities in our study was higher than Rh incompatibility.

In ABO incompatibility, severity of hemolytic disease is very less, and neonatal hyperbilirubinemia remains within physiological limit. It is easily reversible, with minimal morbidity, and without any mortality as seen in the present study.

If ABO incompatibility is present with aggravating conditions, which affect bilirubin level, bilirubin level will rise more than clinically accepted range. It becomes clinically significantly morbid, and results in higher degree of morbidity. e.g., dehydration, infection, cephalhematoma, pre-term babies etc. Neonates with such aggravating conditions were excluded from our study.

According to the population and race, distribution of the blood groups A, B, O and AB varies across the world. One study showed almost a double-fold (38%) ABO incompatibility frequency when compared with Caucasian populations, which showed about one fifth of all pregnancies (20%) having ABO incompatibility between fetus and mother.(12)

This study demonstrated the predominance of blood group O and Rh positivity in both the neonates and their mothers. These findings are in accordance with studies in Nigeria as documented by Bakare et al. in Ogbomosho, South West, Nigeria, and Pennap et al. in Keffi, North Central Nigeria (13,14) also, both sex newborns Male and female were equally affected in our study.

The frequency of Rh D-negative status is much lower, in people of Asian descent (including people from China, India, and Japan), averaging about 2% (10). Rh hemolytic disease is still commonly seen in many developing countries, including India, and it is likely that inadequate prenatal care or failure to administer Rh Ig is responsible for this. It is more common in 'O' blood group mothers, because 'O' blood group mothers have high titers of IgG, than 'A' or 'B' group mothers. In my study, we analyzed ABO group incompatibility, and found that, in them, hyperbilirubinemia was present, but majority did not require any treatment. They had no any significant clinical morbidity. The occurrence of IgG anti-A or anti-B antibodies, in type O mothers, also explains why hemolysis caused by ABO incompatibility, frequently occurs during the first pregnancy, without prior sensitization.

Rh hemolytic disease, rarely occurs during the first pregnancy. However, once sensitization occurs, re exposure to Rh(D) RBCs in subsequent pregnancies leads to an anamnestic response and there is a rise in the maternal anti-D titer, and an increased incidence of affected infants We determined that for HDN of the new-born, due to ABO incompatibility, gravidity does not appear to be a major criterion; Nor does the mode of delivery play any role in development of NNH in this study.

Treatment modality in ABO incompatibility group majority of new born with hyperbilirubinemia no treatment was required while 41.1% neonates were treated with phototherapy along with Rh incompatibility neonates.

Hyperbilirubinemia of varying degrees was demonstrated where these incompatibilities were found; however, no statistical difference was noticed among those with ABO or Rh incompatibilities. Other risk factors for neonatal hyperbilirubinemia were not considered in these studies such as neonatal sepsis and enzymopathies could coexist with the blood group incompatibility; however, Kaplan et al. reported no difference in the degree of hyperbilirubinemia even in the presence of these risk factors (15).

Frequency of ABO incompatibility, 33.33% in this study is in contrast to 7.6% reported by Israel-Aina and Omoigberale in Benin (16) This marked difference may not be unconnected to the size of our study population.

Similar to the frequency found in our study, Manning et al. study in the United Kingdom and several other researchers in Canada and Turkey, reported ABO incompatibility as the most common cause of neonatal jaundice followed by Rh incompatibility and G6PD deficiency (17-19) This report may also be a result of the few Rh-negative individuals as well as the low prevalence of G6PD deficiency in these countries (17-19)

Introduction of anti-D and increase awareness has reduced the spectrum of HDN over the past few decades in Europe and America shifting attention to other allo-antibodies which could be the cause of the emerging HDN being encountered in developed societies. The low prevalence of Rh incompatibility observed in this study is not

surprising due to increase awareness and antenatal clinic attendance as well as the few Rh-negative women in Indian populations.

Neonatal sepsis, G6PD deficiency, and other causes of neonatal jaundice may be responsible for the hyperbilirubinemia seen in the other neonatal population not accounted for in this study.

CONCLUSION

ABO and Rh blood group distribution in this study closely reflect the global distribution of blood groups, while ABO incompatibility has been shown to be a relatively common occurrence among mothers and neonates in our environment compared to Rh incompatibility. Most common cause of hyperbilirubinemia is ABO incompatibility. Most cases of ABO incompatibility develop jaundice, which remains in physiological limits. Due to development of immunological prophylaxis, hemolytic disease due to Rh incompatibility have decreased drastically. The cases which develop hyperbilirubinemia, due to Rh incompatibility, are associated with increased morbidity and mortality. Even with most vigilant and effective antenatal screening protocols, it is not possible, either to predict or forecast which patients couple will deliver a fetus that will develop ABO incompatibility hyperbilirubinemia. The incompatibility reaction, as well, cannot be averted. As a result, this type of hyperbilirubinemia becomes a routine post-natal neonatal affliction, which, whenever indicated, or required, needs to be actively treated, and managed.

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