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Original Research Article

Outcome of neonatal jaundice in term neonates with ABO incompatibility at tertiary level center

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ABSTRACT

Background: Neonatal jaundice is extremely common as almost every new-born develops an unconjugated serum bilirubin level of more than 1.8 mg/dl during the first seven days of life. ABO incompatibility is associated in about 20% of all pregnancies but manifestations of ABO haemolytic disease of new-born occurs in <10% of these cases. True incidence of ABO incompatibility, particularly in developing countries like Nepal, is not understood sufficiently. Furthermore, the confirmation of severe ABO incompatibility cannot be made accurately using only a single test. Hence, this study was done to know the outcome of jaundice in ABO incompatibility patients.
Methods: This was a descriptive cross-sectional study done at Department of Paediatrics, between August 2018 to July 2019. All term neonates born to 'O' positive mother, with blood group A or B positive, and fulfilling the selection criteria were included in the study. Sample size was calculated to be 114 with confidence level at 95% and prevalence of ABO haemolytic disease as 11.4% with margin of error 5%.
Results: Severe ABO incompatibility as evident by presence of jaundice within 24 hours of life, a positive result on direct coomb's test and haemolytic picture on peripheral blood smear was observed in 12% of the total enrolled 200 neonates. Modalities of treatment showed significant relation with severe ABO incompatibility indicating increased need for double volume exchange transfusion in neonates with severe ABO incompatibility.
Conclusions: Phototherapy was found to be effective in the management of most of the cases of neonatal jaundice in term ABO incompatible neonates but some cases, requiring exchange transfusion can occur, mostly in presence of positive result on direct Coomb's test.

Keywords: ABO incompatibility, DCT, Neonatal jaundice, Phototherapy

INTRODUCTION

Neonatal jaundice is extremely common as almost every new-born develops an unconjugated serum bilirubin level of more than 1.8 mg/dl during the first seven days of life.[1] Approximately 60% term and 80% preterm neonate develops jaundice in the first seven days of life.[2] Jaundice in new-born is unique because rise in serum bilirubin is toxic to the neonate's developing central nervous system.[3]

ABO incompatibility is associated in about 20% of all pregnancies but manifestations of ABO haemolytic disease of new-born occurs in <10% of these cases.[4,5] Although haemolytic disease can result in new-born with A, B or AB blood group in which the mother is O group.[1] ABO incompatibility, almost exclusively occurs in babies of blood group A and B of O positive mothers. These new-borns have a high risk of severe neonatal jaundice.[1]

Neonatal jaundice is among the leading cause of morbidities requiring hospital admission among the neonates. Almost every neonate develops jaundice in the neonatal period but pathological jaundice leading to severe elevation in serum bilirubin level is hazardous for the

neonate's developing central nervous system. True incidence of ABO incompatibility, particularly in developing countries like Nepal, is not understood sufficiently. Furthermore, the confirmation of severe ABO incompatibility cannot be made accurately using only a single test. Several tests may be required, which is a challenge in itself, in the settings of resource limited areas in our country. The variable clinical course of the disease adds further burden in its management. Early reorganization, of high-risk cases is, therefore, necessary for timely identification and implementation of treatment measures in order to prevent serious complications. This study was, therefore, commenced to understand the various aspects of neonatal jaundice in ABO incompatible neonates, in terms of its severity and outcome associated with various treatment modalities.

METHODS

Study design and setting

This was a descriptive cross-sectional study done at Department of Pediatrics, Neonatal Intensive Care Unit, Nursery, General pediatric ward and Postnatal wards. This study was conducted for one year from August 2018 to July 2019.

Study population

All term neonates born to 'O' positive mother, with blood group A or B positive, and fulfilling the selection criteria were included in the study. Sample size was calculated to be 114 with confidence level at 95% and prevalence of ABO hemolytic disease as 11.4% 6 with margin of error 5%.

Inclusion criteria

Study had following inclusion criteria: mother with blood group O positive, new-born with Gestational age 37 to 42 completed weeks, new-born with Blood group A or B without Rhesus incompatibility, neonate's mother or legal guardian, willing to participate in this study with written consent.

Exclusion criteria

Our study had following exclusion criteria: new-born with other known causes of jaundice or hemolysis (Rhesus incompatibility, Hypothyroidism, Asphyxia, Sepsis, Cephalhematoma), new-born with conjugated neonatal jaundice, new-born with severe congenital malformations (Spina bifida, encephalocele, anencephaly, gastroschisis, omphalocele or birth trauma).

Operational definitions for this study

ABO incompatibility: Refers to serological evidence of blood group incompatibility between mother and neonate with mother being 'O' positive and neonate being either A positive or B positive.

Severe ABO incompatibility: Refers to neonatal jaundice in ABO incompatible neonates with onset of jaundice within 24 hours, a positive direct coomb's test, and hemolytic picture on peripheral blood smear.

Mild ABO incompatibility: Refers to neonatal jaundice in ABO incompatible neonates in absence of evidence of severe hemolysis.

Direct Coomb's test result: Refers to the observation of a positive or a negative test result of Direct Coomb's test (DCT) as estimated by Automated Gel-Card (Tulip) method.

Peripheral blood smear result: Refers to these two, below mentioned findings, interpreted after performing a Slide preparation method, and using Oil immersion light microscopy for analysis:

- Normal- normocytic, Normochromic blood picture.
- Hemolytic- presence of polychromasia, fragmented red blood cells or spherocytes on peripheral blood picture.

Blood was sent for complete blood count (CBC), C reactive protein (CRP) titer, blood culture and sensitivity (for sepsis screening), reticulocyte count, DCT, PBS (for evidences of hemolysis that aids in the diagnosis of ABO hemolytic disease), thyroid stimulating hormone (TSH) (for evidences of other causes of neonatal jaundice). Serum bilirubin measurements was done 12 hourly, and when required, until 24 after stopping the phototherapy.

Data management and analysis

Researcher enrolled the neonates fulfilling the inclusion criteria and filled the proforma after interviewing the mother and obtaining laboratory investigations.

Statistical analysis was made with MS Excel 2007 (Microsoft Inc.) and Statistical package for the social sciences (SPSS) 21 (IBM Corp.). The data was analyzed using SPSS software version 21 for windows. The descriptive statistics like frequency distribution, mean and percentage were calculated using descriptive statistics and chi square test and fisher's exact test was used to determine the association.

RESULTS

Among the 200 enrolled cases, 104 (52%) of the neonates were male and 96 (48%) were female. The male: female ratio was 1.08:1. Ninety-seven (48.5%) of the cases were early term neonates with gestational age of 37 to 38 weeks.

Blood group O and A incompatibility was more common in this study with the number of neonates with blood group

A positive was 103 (51.5%) and 97 (48.5%) neonates had B positive blood group.

Table 1: Distribution of the neonates according to Socio-demographic factors.

Socio-demographic factors	Frequency	Percentage
Gender		
Male	104	52
Female	96	48
Gestational age (in weeks)		
37-38	97	48.5
39-40	87	43.5
41-42	16	8
Baby blood group		
A positive	103	51.5
B positive	97	48.5

Table 2: Distribution of the neonates according to criteria for diagnosis of severe ABO incompatibility.

Socio-demographic factors	Frequency	Percentage
Onset of jaundice		
<24 hours of life	25	12.5
≥ 24 hours of life	175	87.5
Direct Coomb's test		
Positive	24	12
Negative	176	88
Peripheral blood smear		
Haemolytic	24	12
Normal	176	88

The total serum bilirubin at the onset of jaundice was between 10 to 15 mg/dl in most of the neonates i.e., 108 neonates (54%). 90 (45%) neonates also had total serum bilirubin between 15 to 20 mg/dl which was followed by 2 neonates with total serum bilirubin of less than 10 mg/dl. The mean initial serum bilirubin level in this study was 14.6 mg/dl.

In this study, anemia (considered when hemoglobin level was less than 15 mg/dl), was observed in 15 (7.5%) neonates and all the neonates had evidence of ABO hemolytic disease. However, anemia was not observed in 185 (92.5%) of the enrolled neonates. Positive direct coomb's test result was observed in 24 (12%) neonates. Severe ABO incompatibility as evident by presence of jaundice within 24 hours of life, a positive result on direct coomb's test and hemolytic picture on peripheral blood smear was observed in 12% of the total enrolled 200 neonates.

Phototherapy only was required in 196 (98%) neonates while 4 (2%) neonates required double volume exchange transfusion along with phototherapy as their mode of treatment. Modalities of treatment showed significant relation with severe ABO incompatibility indicating increased need for double volume exchange transfusion in neonates with severe ABO incompatibility. However, statically significant association could not be interpreted as one of the cell values was zero.

In this study, longer duration of phototherapy was required in neonates with severe ABO incompatibility however, statically significant association could not be interpreted as one of the cell values was zero.

All of the 4 neonates requiring double volume exchange transfusion also required phototherapy of 72 hours duration as the mode of treatment in this study. There was no mortality during the period of this study.

DISCUSSION

This study was conducted with the aim to evaluate the outcome of neonatal jaundice in term ABO incompatible neonates. This study aimed to determine the association of severe ABO incompatibility with modalities of treatment used and the duration of phototherapy needed for management of neonatal jaundice in such neonates.

Among the 200 enrolled cases, 104 (52%) of the neonates were male and 96 (48%) were female. The male: female ratio was 1.08:1. Similar finding was observed in Singh R et al with 55% of male and 41% of female new-born among the total of 240 enrolled cases.[7] Similarly, in Akgül et al, among the 166 term neonates, 54.2% were male and 45.8% were female new-borns.[8]

Ninety-seven children (48.5%) of the cases were early term neonates with gestational age of 37 to 38 weeks similar to study by Singh et al.[7] OA blood group incompatibility was more common, similarly to study by Akgül et al.[8]

Anemia was observed in 15 (7.5%) neonates. Similar, finding was also observed in Ella et al, which stated anemia to be a known symptom among neonates with ABO hemolytic disease.[9] Kattimani et al also found anemia to be associated with 18% of cases among the total 50 enrolled cases of ABO hemolytic disease suggesting an increased association of anemia in ABO hemolytic disease.[10] Positive direct coomb's test result was observed in 24 (12%) neonates. DCT positivity was 8% to 18.2% in study by different authors.[8,10,11] Hemolytic picture on peripheral blood smear was observed in 24 (12%) neonates. Similar, observation was also made in Akgül et al who found hemolytic picture on peripheral blood smear in 14.5% cases.[8] Much higher incidence was found in Kattimani et al that documented 44% neonates with micro spherocytes on peripheral blood smear representing hemolytic picture.[10]

Regarding the mode of treatment, Phototherapy only was required in 196 (98%) neonates while 4 (2%) neonates required double volume exchange transfusion along with phototherapy as their mode of treatment. Kattimani et al

supports this observation as 98% of the 50 cases in his study required phototherapy and exchange transfusion was required in 2% of cases.[10] Similarly, in Begum et al exchange transfusion was required as a mode of treatment in 1.3% cases while 78% cases were treated with phototherapy.[12]

Severe ABO incompatibility as evident by presence of jaundice within 24 hours of life, a positive result on direct Coomb's test and hemolytic picture on peripheral blood smear was observed in 12% of the total enrolled 200 neonates. Similar observations were also made in Ella et al and Singh et al that document the prevalence of severe ABO incompatibility to be 10 % and 17% respectively.[7,9] However, even much higher prevalence was observed in Sarici S Ü et al that documents severe ABO incompatibility to occur in 21.3% of the enrolled neonates.[13]

Table 3: Association of severe ABO incompatibility with socio-demographic factors; gender, baby blood group.

Variables	Severe ABO incompatibility (%)	Mild ABO incompatibility	χ^2	P value
Gender				
Male	15 (62.5)	89 (50.6)	1.205	0.272
Female	9 (37.5)	87 (49.4)		
Baby blood group				
A positive	12 (50)	91 (51.7)	0.025	0.875
B positive	12 (50)	85 (48.3)		

Table 4: Association of severe ABO incompatibility with mode of treatment.

Variables	Severe ABO incompatibility (%)	Mild ABO incompatibility (%)	P value
Mode of treatment			
Phototherapy	20 (83.3)	176 (100)	—
DVET + phototherapy	4 (16.7)	—	

Modalities of treatment showed significant relation with severe ABO incompatibility indicating increased need for double volume exchange transfusion in neonates with severe ABO incompatibility. However, statically significant association could not be interpreted as one of the cell values was zero. Statically significant association was observed in Akgül et al which demonstrated 10.8% of the cases requiring exchange transfusion and 10.8% of the cases requiring IVIG as the modalities of treatment while phototherapy was required in only 78.4% of the cases.[8] Similarly, Sharma et al documented need for exchange transfusion in 6 out of 6 neonates with ABO haemolytic disease with their total serum bilirubin level of 22 to 26.8 mg/dl, thus, advocating for the severe nature of ABO incompatibility and need for invasive methods like exchange transfusion in the treatment of neonatal jaundice in term ABO incompatible neonates.[14]

In this study, longer duration of phototherapy was required in neonates with severe ABO incompatibility however, statically significant association could not be interpreted as one of the cell value was zero. The need for longer duration of phototherapy treatment was also supported by the findings from Osborn LM et al that states the mean duration of phototherapy required in ABO haemolytic disease to be 78.5 hours.[15] Similarly, Gopu S Begum A et al and Kattimani VS et al also observed need for longer duration of phototherapy with mean duration of phototherapy in their study to be approximately 54 hours and 53.84±9.82 hours respectively.[10,12] All of the 4 neonates requiring double volume exchange transfusion also required phototherapy of 72 hours duration as the mode of treatment in this study.

There was no mortality during the period of this study. Similar, finding was also observed in Begum et al, Akgül et al, and Kattimani et al which does not document any observation of mortality due to neonatal jaundice in term ABO incompatible neonates.[8,10,12]

CONCLUSION

The present study showed that the prevalence of severe ABO incompatibility among term ABO incompatible neonates were 12%. It was also noted that phototherapy, as a mode of treatment was found to be effective in the management of most of the cases of neonatal jaundice in term ABO incompatible neonates but some cases, requiring exchange transfusion can occur, mostly in presence of positive result on direct coomb's test. However, longer duration (≥48 hours) of phototherapy treatment was required in neonates with evidences of severe ABO incompatibility. Minor blood group incompatibility was not evaluated in this study, making it the limitations of this study as immune haemolysis due to minor blood group mismatch can occur leading to neonatal jaundice.

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