Pak J Med Res
Vol. 55, No. 4, 2016

Original Article

ABO Incompatibility in Neonates Coming to a Pediatric Tertiary Care Hospital

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Abstract

Background: ABO hemolytic disease is the most frequent cause of neonatal jaundice.
Objectives: To determine the frequency of ABO incompatibility causing jaundice in neonates coming to a pediatric public sector hospital.
Study design, settings and duration: Cross-sectional study conducted at National Institute of Child Health (NICH), Karachi, from 2nd August 2013 to 1st August 2014.
Patients and Methods: All neonates of both gender, having serum indirect bilirubin >13 mg/dl and born to mothers having O positive blood group who came to the hospital during the study period were enrolled. Detailed history and physical examination was done in all. Mean± SD were calculated for qualitative variables and categorical variable as frequency and percentages. Chi square test and p-value < 0.05 was taken as significant. Data was analysed in SPSS version 19.
Results: A total of 170 neonates were included comprising of 96 male and 74 females. Their mean age was 9.56 ± 2.69 days, mean time of onset of jaundice was 2.86 ± 0.78 days and mean indirect serum bilirubin level was 14.86 ± 1.59 mg/dl. Though all mothers were O positive but the blood group of neonates varied. Majority (72.3%) had blood group O+ followed by B+ (38.2%), A+ (34.0%) and AB+ (27.6%)**.** Among mothers with O+ blood group, the ABO incompatibility was observed in 47 (23.5%) neonates. There was no significant association of ABO incompatibility with gender, age, onset of jaundice and indirect serum bilirubin level ($p > 0.05$).
Conclusion: ABO incompatibility as a common cause of jaundice was seen in 23% neonates.
Key words: ABO incompatibility, neonatal jaundice, blood group.

Introduction

Neonatal jaundice is a frequent cause of morbidity in newborns worldwide and the most frequent cause of hospitalization and readmission in the initial week of life,[1-3] affecting 60% of term and 80% of preterm neonates.[4] Recent global estimates indicate that yearly around 1.1 million neonates would develop significant neonatal jaundice which shall be mostly seen in sub-Saharan Africa and South Asia.[5] Available evidence also focus on the impact of severe neonatal jaundice with or without bilirubin encephalopathy, in causing substantial mortality and its long-term impact on health in low and middle income countries.[6-8] Hemolytic disease of newborn, and various etiologies of neonatal jaundice has been recognized as a distinct cause of neonatal morbidity and mortality by the WHO and the Global Burden of Disease Collaborators.[9,10] Risk factors of neonatal jaundice includes hemolysis secondary to Rhesus isoimmunisation and ABO incompatibility, sepsis, prematurity and enzyme defects (Uridyl diphosphate glucoronyl transferase enzyme deficiency).[11]

Hemolytic disease of the newborn is characterized by immune mediated hemolysis of the neonatal red cells by the maternal antibodies via transplacental route. The culprit antibodies are either naturally occurring (anti A, anti B) or immune mediated antibodies resulting from sensitizations after transfusion or pregnancy.[12] There are over 60 RBC antigens that are responsible for an antigen antibody response, but the Rh group with its D antigen and ABO incompatibility remains the most significant cause of hemolysis in neonates. Among the total live births, 15% are at risk, while the disease manifests in only 0.3 - 2.2% of neonates.[4]

ABO incompatibility constitutes an antibody reaction that occurs due to different mother and baby blood groups, typically when mother blood group is O, and baby blood group being either A or B. ABO

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Received: 12 April 2016, **Accepted:** 10 September 2016,
Published: 15 December 2016

Authors Contribution

MK conceived, designed, editing, statistical analysis and final approval of the manuscript. KAM did critical revision, drafting, net searching and editing of the manuscript. UH did data collection editing and statistical analysis.

hemolytic disease characterizes neonatal jaundice with a positive coombs test against the A or B antigens in babies born to mothers with blood group O.[13] Anti-A and anti-B are Immunoglobulin G (IgG antibodies) most frequently seen in individuals with blood group O.[14] For infants delivered at or after 35 weeks of gestation ABO incompatibility is the most prominent risk factor for significant neonatal jaundice.[15]

National Institute of Child Health Karachi, is a tertiary care hospital that caters for a huge population of jaundiced neonates coming from urban and rural areas of Sindh and part of Baluchistan. This study aims to identify current practices and challenges for the effective management of infants with clinically significant neonatal jaundice and to identify the gaps in their management.

Patients and Methods

The National institute of child Health (NICH) is a tertiary care public sector Pediatric hospital which deals with a large number of neonates yearly for a spectrum of disorders including neonatal jaundice. This cross-sectional study was conducted at neonatal unit of NICH, for a period of 1 year from 2nd August 2013 to 1st August 2014). All neonates of either gender coming with jaundice and having serum bilirubin 13 mg/dl or greater and born to mothers having O positive blood group were included in the study. Neonates with congenital anomalies and syndromes, Rh incompatibility and G6PD deficiency were excluded. Sample size was calculated using WHO sample size calculator. Using the previously reported prevalence of ABO incompatibility in neonatal jaundice as 20% [16] and with 6% margin of error 95% confidence and 10% refusal rate, a sample size of 183 neonates was calculated.

Approval from institutional ethical review committee was taken. Neonates were enrolled in the study after taking informed consent from the parents/guardians. Demographic data on name, age, gestational age, gender, birth weight and hospital registration number was collected on a profroma. Infant's age was recorded in hours and days. After taking history and performing physical examination, blood tests were run for complete blood count, peripheral smear, reticulocyte count, coombs test, serum bilirubin, mother and baby's blood group. All babies were managed as per standard protocol of the hospital. Phototherapy was started when bilirubin level was around 13mg/dl and exchange transfusion was done when bilirubin level was over 20mg/dl. The data was entered in Epi Data (version 3.2) and errors removed and the clean data was converted into SPSS (version 19.0). Mean ± standard deviation were calculated for age & serum bilirubin. Categorical variables like gender, ABO incompatibility were described as frequency and percentages. Confounding variables like age, gender, time of onset of jaundice and serum bilirubin (indirect) were controlled by stratified analysis. Chi square test was applied for significance.

Results

A total of 170 neonates were admitted with neonatal jaundice due to ABO incompatibility in the study period. There were 96 males and 74 females whose mean age was 9.56 ± 2.69 days (range 4 - 17) (Figure-1). Majority (71.2%) were ≤ 10 days of age while 28.8% were > 10 days of age. The mean age of patients was calculated in the above mentioned groups.

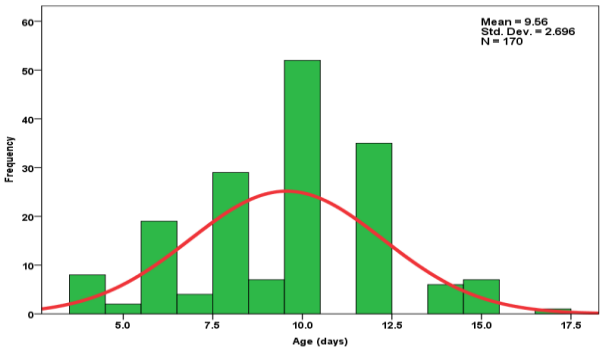

Figure 1: Histogram presenting distribution of age (days).

The mean age at the time of onset of jaundice was 2.8 ± 0.78 days (range 1 - 5 days). Mean Hemoglobin was 12.2 ± 1.3 gm/dl (range 9.6-16.2).Their mean serum bilirubin level was 16.5 ± 1.59 mg/dl (9.6 - 14.1) with mean indirect serum bilirubin of 14.8 ± 1.5 mg/d (range 11.9 - 22.5).The indirect serum bilirubin was divided in two groups (Figure-2). Ten neonates 10 (5.9%) had indirect serum bilirubin > 17.5 while 160 (94.1%) had values ≤ 17.5. Phototherapy was given to all neonates while exchange transfusion was performed in 5% who had total serum bilirubin ≥ 20 mg/dl.

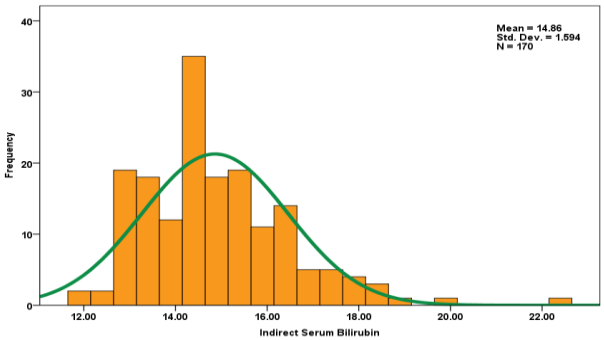

Figure 2: Histogram presenting indirect serum bilirubin level (mg/dl).

The frequency of blood groups in neonates were 34.0% A+, 38.2% B+, 27.6% AB+ and 72.3% O+. Among mothers with O+ blood group, the ABO incompatibility was observed in 47 neonates who had either blood group A+ or B+ or AB+, while 123 had no incompatibility.

The descriptive analysis of neonate's age, age at onset of jaundice, total serum bilirubin and indirect serum bilirubin in those having ABO incompatibility and those without incompatibility is shown in Tables 1 & 2.

Table 1: Descriptive statistics of patients with ABO incompatibility.

Variables	*Mean*	*SD*	*Min*	*Max*	*Range*
Age (days)	9.72	2.79	4	17	13
Age of Onset Jaundice (days)	2.85	0.80	1	4	3
Total Serum Bilirubin (mg/dl)	16.35	1.59	14.10	20.20	6.1
Indirect Serum Bilirubin (mg/dl)	14.69	1.58	11.90	19.80	7.9
Hemoglobin (gm/dl)	12.29	1.37	9.60	16.20	6.6

Table 2: Descriptive statistics of patients without ABO incompatibility.

Variable	*Mean*	*SD*	*Min*	*Max*	*Range*
Age (days)	9.36	2.58	4	15	11
Age of Onset Jaundice (days)	2.87	0.76	2	5	3
Total Serum Bilirubin (mg/dl)	16.80	1.57	14.40	23.76	9.36
Indirect Serum Bilirubin (mg/dl)	15.06	1.58	12.40	22.50	10.1
Hemoglobin (gm/dl)	12.23	1.43	9.60	16.20	6.6

The ABO incompatibility was seen in 51 (54.8%) male and 42 (45.2%) female neonates and showed no association of ABO incompatibility with gender ($p > 0.05$). ABO incompatibility was observed in 66 (71.0%) neonates aged ≤ 10 days and in 27 (29.0%) aged > 10 days with no significant association of ABO incompatibility with age ($p > 0.05$).

ABO incompatibility was observed in 75 (80.6%) neonates aged ≤ 3 days and in 18 (19.4%) aged > 3 days and again showed no significant association of ABO incompatibility with age at onset of jaundice ($p > 0.05$).

ABO incompatibility was observed in 86 (92.5%) neonates having indirect serum bilirubin level ≤ 17.5 mg/dl and in 7 (7.5%) with indirect serum bilirubin level > 17.5 mg/dl (not significant). None of the jaundiced neonates developed kernicterus.

Discussion

In the present study, out of 170 mothers having blood group O +ve, 47 (27.6%) neonates had ABO incompatibility resulting in neonatal jaundice. ABO incompatibility has been reported in 15 - 25% pregnancies having varied profile of hemolytic disease, out of which approximately 10% newborns manifest with clinically significant neonatal jaundice.[17,18] It constitutes hemolysis of milder intensity than the hemolytic disease resulting from Rh incompatibility. Frequent presentation includes jaundice in the first day of life, high bilirubin levels requiring interventions reticulocytosis in the peripheral blood smear suggesting hemolysis. Phototherapy alone is quite effective therapy to treat high levels of bilirubin and rarely exchange transfusions, intravenous immunoglobulin (IVIG) administration, or transfusions with packed red blood cells are required. However, literature does mention, significant ABO hemolytic disease characterizing significant anemia secondary to severe hemolysis , needing blood transfusions.[19,20]

Globally, East Asians have a strong susceptibility to neonatal jaundice.[21] Most studies done on ABO incompatibility have been done on Caucasian infants and have shown variable frequencies. One report concluded that the incidence of ABO incompatibility and hemolytic disease in a new born was 2 - 3 times greater in Africa-Americans as compared to Caucasians.[22] ABO incompatibility in Czech republic and Venezuela were 14% and 16% respectively.[23,24] A study in Makkah reported ABO incompatibility of 12%.[25] One worker reported ABO incompatibility as the commonest cause of neonatal jaundice with incidence of 22.1%, mean serum bilirubin level of 25.9 ± 7.5 mg/dL in neonates aged 4.4 ± 2.1 days.[26] Our study showed the frequency of ABO incompatibility in neonatal jaundice to be 27.6% with mean serum bilirubin of 16.5 ± 1.5 mg/dl and mean age of onset of jaundice as 2.86 ± 0.78 days.

In ABO incompatibility, hemolysis is of benign nature rarely resulting in significant jaundice and anaemia.[27] In our study mean Hemoglobin was 12.2 ± 1.3gm/dl.

In a study, infants were recognized to be at risk of developing hemolytic disease secondary to ABO incompatibility, when they had a positive direct antiglobulin test. The study further established that BO incompatibility (21.5%) was more common than AO (14.8%) and more in black (18.8%) vs. nonblack (10.8%) infants.[28] Similar were our findings where BO incompatibility was 38.2% and AO incompatibility was 34.0% but all our neonates were of Asian origin.

Conflict of interest: None declared.

References

1. Burke BL, Robbins JM, Bird TM, Hobbs CA, Nesmith C, Tilford JM. Trendsin hospitalizations for neonatal jaundice and kernicterus in the United States, 1988‑2005. Pediatrics 2009; 123: 524‑32.
2. National Institute for Health and Clinical Excellence. Neonatal Jaundice. (Clinical Guideline 98); 2010. (Accessed on 11th November 2016) Available from URL: https://www.nice.org.uk/CG98.

3. Young Infants Clinical Signs Study Group. Clinical signs that predict severe illness in children under age 2 months: A multicentre study. Lancet 2008; 371:135‑42.
4. Maheshwari A, Carlo WA. Hemolytic disease of the newborn (Erythroblastosis fetalis) Nelson Textbook of pediatrics. 20 th ed. Philadelphia: Saunders, 2016: 883-7.
5. Bhutani VK, Zipursky A, Blencowe H, Khanna R, Sgro M, Ebbesen F. Neonatal hyperbilirubinemia and Rhesus disease of the newborn: Incidenceand impairment estimates for 2010 at regional and global levels. Pediatr Res 2013; 74(Suppl 1):86‑100.
6. Olusanya BO, Ogunlesi TA, Slusher TM. Why is kernicterus still a major cause of death and disability in low‑income and middle‑income countries? Arch Dis Child 2014; 99: 1117‑21.
7. Slusher TM, Olusanya BO. Neonatal jaundice in low‑ and middle‑incomecountries. In: Stevenson DK, Maisels J, Watchko J, eds. Care of the Jaundiced Neonate. New York: McGraw‑Hill, 2012, pp 263‑73.
8. Maulik PK, Darmstadt GL. Childhood disability in low‑ and middle‑incomecountries: Overview of screening, prevention, services, legislation, andepidemiology. Pediatrics 2007; 120 (1): 51‑5.
9. Bhutani VK, Zipursky A, Blencowe H, Khanna R, Sgro M, Ebbesen F. Neonatal hyperbilirubinemia and Rhesus disease of the newborn: Incidence and impairment estimates for 2010 at regional and global levels. Pediatr Res 2013; 74 (1): 86‑100.
10. GBD 2013 Mortality and Causes of Death Collaborators. Global, regional and national age‑sex specific all‑cause and cause‑specific mortality for 240 causes of death, 1990‑2013: A systematic analysis for the Global Burden of Disease Study 2013. Lancet 2015; 385: 117‑71.
11. Israel-Aina YT, Omoigberale AI. Risk factors for neonatal jaundice in babies presenting at the University of Benin Teaching Hospital, Benin City. Nigerian J Paediatr 2012; 39(4): 159-63.
12. Basu S, Kaur R, Kaur G. Hemolytic disease of the fetus and newborn: Current trends and perspectives. Asian J Transfus Sci 2011; 5(1): 3-7.
13. Saluja S, Kleer N, Soni A, Garg P, Saxena U. Exchange transfusion through peripheral vessels. J Neonatol 2000; 1: 52-5.
14. Murray NA, Roberts IA. Haemolytic disease of the newborn. Arch Dis Child Fetal Neonatal Ed 2007; 92: 83–8.
15. Yogev-Lifshitz M, Leibovitch L, Schushan-Eisen I, Taran C, Strauss T, Maayan-Metzger A. Indication of mild hemolytic reaction among preterm infants with ABO incompatibility. Pediatr Blood Cancer 2016; 63(6): 1050-3.
16. Maisels MJ. Neonatal jaundice. Pediatr Rev 2006; 27: 443-54.
17. Akgül S, Korkmaz A, Yiğit S, Yurdakök M. Neonatal hyperbilirubinemia due to ABO incompatibility: does blood group matter? Turk J Pediatr. 2013; 55(5): 506-9.
18. Bhat YR, Kumar CG. Morbidity of ABO haemolytic disease in the newborn. Paediatr Int Child Health 2012; 32(2): 93-6.
19. Ziprin JH, Payne E, Hamidi L, Roberts I, Regan F. ABO incompatibility due to immunoglobulin G anti-B antibodies presenting with severe fetal anaemia. Transfus Med 2005; 15: 57–60.
20. Senterre T, Minon JM, Rigo J. Neonatal ABO incompatibility underlies a potentially severe hemolytic disease of the newborn and requires adequate care. Arch Pediatr 2011; 18: 279–82.
21. Setia S, Villaveces A, Dhillon P, Mueller BA. Neonatal jaundice in Asian, white, and mixed-race infants. Arch Pediatr Adolesc Med 2002; 156: 276-9.
22. Bucher KA. Racial difference in incidence of ABO-hemolytic disease. Am J Public Health 1976; 66: 854-58
23. Hodr R. ABO hemolytic disease; sex ratio and blood groups in newborns requiring treatment. Czech Med 1989; 12(3): 25-33.
24. Cariani L, Romano EL, Martinez N, Mobano R, Suarez G, Ruiz I, Sovano A: ABO hemolytic disease of the newborn (ABO-HDN): factors influencing its severity and incidence in Venezuela. JTrop Pediatr1995; 41(1): 14-21.
25. Alkhotani A, Mohamed NourEldin EE, Zaghloul A,Mujahid S. Evaluation of neonatal jaundice in the Makkah region. Scientific reports 2014; 4: 4802.
26. Badiee Z. Exchange transfusion in neonatal hyperbilirubinaemia: experience in Isfahan, Iran. Singapore Med J 2007; 48: 421-3.
27. Ziprin JH, Payne E, Hamidi L, Roberts I, Regan F. ABO incompatibility due to immunoglobulin G anti-B antibodies presenting with severe fetal anaemia. Transfus Med 2005; 15(1): 57-60.
28. Özgönenel B, KukrejaG, O'MalleyB, Bluth MH. Neonatal BO Incompatibility Is Associated With a Positive Cord Blood Direct Antiglobulin Test in Infants of Black Ethnicity. J Pediatr Hematol Oncol 2015; 37(8): e453-7.