PREVALENCE OF RHESUS TYPE AND ABO INCOMPATIBILITY IN JAUNDICED NEONATES

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ABSTRACT

Objective: *To determine the prevalence of Rh and ABO incompatibility in jaundiced neonates.*

Methodology: *This hospital based descriptive study was conducted in Pediatrics Unit, Lady Reading Hospital Peshawar. A total of 200 neonates with clinically diagnosed jaundice were included in the study.*

Results: *Out of 200 neonates 70% were male and 30%female. Majority of neonates 99.5% age was ranged from 0-10 days while only 0.5% neonate was 13 days. Out of 200 neonates, the frequency of ABO-incompatibility and Rh-incompatibility in jaundiced neonates in this study was 22.5% and 12.5% respectively. Out of the remaining 65.5% cases physiological jaundice was diagnosed in 40.5% neonates, prematurity in 15% neonates and G6PD in 9.5% neonates. Among 22.5% cases of ABO incompatibility there were 16.5% males and 6% females. Majority 15% presented on 1st day of life, followed by 3% on 2nd and 3rd day of life respectively, 1% on 4th day, 0.5% on 5th day of life.*

Conclusion: *Out of 200 neonates presented with jaundice, prevalence of ABO-incompatibility was found to be 22.5% followed by Rh-incompatibility 12.5%*

Key Words: *Neonatal jaundice, hyperbilirubinemia, Kernicterus ABO-incompatibility, Rh-incompatibility.*

INTRODUCTION

Neonatal jaundice is defined as yellowish discoloration of skin, sclera of eyeball, and mucous membranes caused by deposition of bile salts in these tissues. Depending upon the cause the jaundice may be present at birth or any time during the neonatal period. Jaundice due to either indirect (unconjugated) or direct (conjugated) bilirubin within the first 24 hours of life should be taken seriously[1].

Neonatal Jaundice (NNJ) is a common disorder worldwide. Early identification and proper management is needed to prevent the serious neurological complications associated with it[2].

Kernicterus or bilirubin encephalopathy is a neurological syndrome which results from the deposition of unconjugated (indirect) bilirubin in the basal ganglia and brain stem nuclei[1].

Hemolytic disease of the newborn (HDN) is a condition in which life span of fetal red blood cells (RBCs) is shortened by the action of maternal antibodies against the antigens present on RBCs. Anti-D is the commonest cause of mild, moderate and severe HDN. Red cells destruction begins in intrauterine life and it leads to severe anemia, hydrops fetalis and death in utero[3].

The most common cause of jaundice in first 24 hours of life due to HDN is rhesus (Rh) hemolytic disease. As the mother becomes sensitized due to fetomaternal transfusions in previous pregnancies, anti-D IgM and IgG are produced. Anti-D IgG is responsible for rhesus disease in the neonate as this antibody can cross placenta. Rhesus (Rh) incompatibility develops between an Rh-negative mother (previously sensitized) and her Rh-positive fetus[4].

ABO incompatibility (mother usually blood group O, infant blood group "A" or "B"), is the most common cause for HDN in the UK and

occurs in 15% of pregnancies. IgG antibody is responsible for this condition also[4]. ABO incompatibility is a common condition in a newborn baby and causes minimal hemolysis. It may cause elevated levels of bilirubin and anemia but less severe than Rh hemolytic disease[5].

In a local study, HDN was diagnosed in 82 cases (20.5%) associated with blood group incompatibility. In this study ABO incompatibility was more common with 58 cases, while Rh-incompatibility was diagnosed in 19 cases[6].

ABO incompatibility occurs in 20% of pregnancies but only 20% of these develop hemolytic disease. In addition to severe jaundice, these infants may also develop significant anemia over the first several weeks of life[7].

Kernicterus is more likely to occur with bilirubin levels higher than 20 mg/dl. The risk of kernicterus is less for full term infants as compared to pre-term infants. Phototherapy and exchange transfusion are the options available to avoid the risk of kernicterus[7].

All the pregnant women should be tested for ABO/Rh type and screened for antibody during the first visit to obstetrician. These initial tests will help to identify women who require anti-immunoglobulin (Rh IG) and further monitoring. Rh IG administration results in greater than 90% reduction in alloimmunization rate among treated women[8].

The purpose of the study was to determine the prevalence of Rh and ABO incompatibility in jaundiced neonates presenting at Department of Pediatrics & Neonatology, Lady Reading Hospital, Peshawar.

METHODOLOGY

This cross sectional study was conducted in Department of Pediatrics and Neonatology, Lady Reading Hospital, Peshawar for one year from April 2009 to March, 2010 on 200 neonates, both male and female with clinically diagnosed jaundice included by consecutive (Non probability) sampling.

Jaundiced neonates with gestational age less than 28 weeks; jaundiced neonates with weight of less than 500 gms; babies with history of drug intake like Moxalactum and Sulfisoxazole and babies whose mothers were hepatitis A IgM positive, HBsAg (hepatitis B surface antigen) positive, and anti-HCV (hepatitis C antibody) positive were excluded from the study.

After getting approval from the hospital ethical committee to conduct the study, data was collected of all those neonates who met inclusion criteria presenting through Out-patient department (OPD) or accident/emergency department and admitted in Pediatrics and Neonatology department of Postgraduate Medical Institute, Lady Reading Hospital, Peshawar. An informed consent was taken from parents or relatives of the neonates for further evaluation. Parents were inquired about the age of presentation of jaundice in the neonates. The skin, sclera of eyeball and mucous membrane was examined for jaundice. The required investigations like serum bilirubin level (total, direct and indirect), blood groups of baby and mother were done in hospital laboratory for the diagnosis of Rhesus (Rh) and ABO incompatibility in jaundiced neonates. All these information and other demographic data like name, age, sex, address, date of admission and date of discharge was also entered into a proforma.

All the qualitative variables like gender, blood groups of baby and mother, diagnostic findings, Rh-incompatibility and ABO-incompatibility were analyzed for percentages and frequencies. Mean $\pm$ standard deviation was calculated for quantitative variables like age and age at the onset of jaundice, weight and serum bilirubin levels (total, direct and indirect). For gender male to female ratio was calculated. The results were presented through tables, cross tabulation, graphs and charts. All the data was stored and analyzed by statistical program SPSS version 12 for windows.

RESULTS

A total of 200 neonates with jaundice were included in the study. Out of 200 neonates 140 (70%) were male while 60 (30%) were female. The overall male to female ratio was 2.33: 1 (Table 1).

In majority of neonates 199 (99.5%) age was ranged from 0-10 days, while only 01 (0.5%) neonate was 13 days. Mean age was 3.5585 $\pm$ 2.5599 days (Table 1).

Out of 200 neonates included in the study, 45 were diagnosed as ABO-incompatibility which makes up 22.5% of the total cases; while 25 neonates were diagnosed as Rh-incompatibility accounting for 12.5% of the total cases. Therefore the frequency of ABO-incompatibility and Rh-incompatibility in jaundiced neonates in this study was 22.5% and 12.5% respectively (Table 1).

Out of the remaining 130 (65.5%) cases physiological jaundice was diagnosed in 81 (40.5%) neonates, prematurity in 30 (15%) neonates and G6PD in 19 (9.5%) neonates.

Cross tabulation of blood grouping of babies and mothers are given in Table 2.

Among the 45 (22.5%) cases of ABO

incompatibility there were 33 (16.5%) males and 12 (6%) females. Majority 30 (15%) presented on 1st day of life, followed by 6 (3%) on 2nd and 3rd day of life respectively, 2 (1%) on 4th day, and 01 (0.5%) on 5th day of life.

Among 25 (12.5%) cases of Rh-incompatibility there were 18 (9%) male and 7 (3.5%) female neonates. Majority 18 (9%) cases presented on 1st day of life, followed by 3 (1.5%) on 2nd day of life, 2 (1%) on 4th day, and 01 (0.5%) on 3rd and 6th day of life respectively (Table 3).

Table 1: Demographic Distribution of Patients (n=200)

Variables	No. of Cases	Percentage
Gender distribution:		
Male	140	70%
Female	60	30%
Age ranges		
0-10 days	199	99.5%
11-29 days	01	0.5%
Frequency of rhesus and ABO-incompatibility:		
ABO-incompatibility	45	22.5%
Rhesus-incompatibility	25	12.5%
01 day	90	45%
02 days	24	12%
03 days	54	27%
04 days	15	7.5 %
05 days	07	3.5%
06 day	03	1.5%
07 days	05	2.5%
08 days	02	01%

Table 2: Cross Tabletion of Blood Groups of Neonates and Mothers

	Blood Groups	Blood Group of Mothers								
		A^+	A^-	AB^+	AB^-	B^+	B^-	O^+	O^-	Total
Blood Group of Neonates	A^+	37	3	2			1	22	1	66
	A^-	3	2							5
	AB^+	3		3		2	1			9
	AB^-				1					1
	B^+		1	3	1	42	6	16	3	72
	B^-					1	1			2
	O^+	6				5	1	23	5	40
	O^-							2	3	5
	Total	**49**	**6**	**8**	**2**	**50**	**10**	**63**	**12**	**200**

Table 3: Cross Tabulation of Sex and Age of Presentation of Jaundice in Neonates (n=200)

	Sex	Age of presentation of jaundice in neonates (in days)								Total
		Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7	Day 8	
ABO-incompatibility	Male	18	6	6	1	2	-	-	-	33
	Female	12	-	-	-	-	-	-	-	12
	Total	**30**	**6**	**6**	**1**	**2**	**-**	**-**	**-**	**45**
Rhesus-incompatibility	Male	14	2	-	2	-	-	-	-	18
	Female	04	1	1	-	-	1	-	-	07
	Total	**18**	**3**	**1**	**2**	**-**	**1**	**-**	**-**	**25**

DISCUSSION

Newborns with jaundice or unrecognized hyperbilirubinemia are a vulnerable population. Of the 4 million infants born each year in the United States, over 3.5 million are born at 35 or more weeks of gestation. Most have benign outcomes with little or no threat of neurological compromise from medical conditions during their first year of life. Nearly all healthy infants have some degree of hyperbilirubinemia and over 60% develop jaundice during their first week of life. When unmonitored or untreated in a timely manner, hyperbilirubinemia can become excessive and may be unrecognized if the infant is not under medical supervision.[9]

Neonatal jaundice is usually harmless, this condition is often seen in infants around the second day after birth, lasting until day 8 in normal births, or to around day 14 in premature births. Serum bilirubin normally drops to a low level without any intervention required: the jaundice is presumably a consequence of metabolic and physiological adjustments after birth. In extreme cases, a brain-damaging condition known as kernicterus can occur, leading to significant lifelong disability. There are concerns that this condition has been rising in recent years due to inadequate detection and treatment of neonatal hyperbilirubinemia. Early treatment often consists of exposing the baby to intensive phototherapy.[10]

Neonatal jaundice is the most common medical problem affecting babies in the first week of life. About 50% of term and 80% of preterm babies develop jaundice, which usually appears 2-4 days after birth and resolves spontaneously after 1-2 weeks. Jaundice is caused by bilirubin deposition in the skin. Most jaundice in newborn infants is a result of increased red cell breakdown and decreased bilirubin excretion[11,12] .

In this study majority of neonates 45% presented with jaundice on day 01 of their life followed by 27% on day 03 of their life. These results are comparable with the studies[11, 12] in which it is also mentioned that neonatal jaundice usually appears 2-4 days after birth.

Hyperbilirubinemia is a common disorder during the neonatal period. It is associated with a variety of physiologic and pathologic conditions. Isoimmune hemolytic disease has been identified as a pathologic cause of neonatal hyperbilirubinemia attributed to blood group incompatibility. Group A and group B newborns of group O mothers are defined as having ABO incompatibility[13]. In our study out of 200 neonates, the prevalence of ABO-incompatibility in jaundiced neonates was 22.5%.

ABO incompatibility and glucose-6-phosphate dehydrogenase (G6PD) deficiency are the most common causes of hemolytic anemia. If these conditions are present, phototherapy and

exchange transfusion may be considered at lower TSB levels because these conditions can cause predictably severe hyperbilirubinemia[14]. G6PD was diagnosed in 9.5% neonates out of 200 neonates included in this study.

In this study out of 200 neonates, the frequency of ABO-incompatibility and Rh-incompatibility in jaundiced neonates was 22.5% and 12.5% respectively. Our results are in agreement with the studies done abroad[14,15] and local studies[6,16]. They all agree that ABO-incompatibility was more prevalent than Rh incompatibility in their studies.

In one study factors associated with severe neonatal jaundice in babies requiring exchange blood transfusion (EBT) included low birth weight (<2500 g, 44.4%), ABO incompatibility (30.0%), glucose-6-phosphate dehydrogenase deficiency (34.4%) and septicemia (26.1%). Twenty-seven (30.0%) neonates developed features of kernicterus; 26 before admission while 1 during admission; all except one were delivered outside the hospital[17].

Jaundice in the newborn is a problem because elevation of serum bilirubin is potentially toxic to infant's developing central nervous system[18].

Neonatal jaundice is the result of an imbalance between bilirubin production and elimination. Bilirubin conjugation in newborns is significantly impaired in the first few days; even a small increase in the rate of production can contribute to the development of hyperbilirubinemia[19]. In our study in 200 neonates with jaundice mean total serum bilirubin was 20.0878 $\pm$ 5.6424. Mean direct serum bilirubin was 2.7711 $\pm$ 4.510. Mean indirect serum bilirubin was 17.9630 $\pm$ 4.6841.

Some 60% of normal newborns become clinically jaundiced sometime during the first week of life. Unconjugated (indirect) hyperbilirubinemia occurs as a result of excessive bilirubin formation and because the neonatal liver cannot clear bilirubin rapidly enough from the blood. Although most newborns with jaundice are otherwise healthy, they need to be monitored because bilirubin is potentially toxic to the central nervous system. Sufficiently elevated levels of bilirubin can lead to bilirubin encephalopathy and subsequently kernicterus, with devastating, permanent neurodevelopmental handicaps[20-22].

Blood type and Coombs' testing should be performed in all infants who are receiving phototherapy or whose bilirubin level is increasing rapidly. In infants with isoimmune hemolysis (ABO incompatibility), the Coombs' test will be positive because the infant's red blood cells are coated with maternal antibodies. These cells will be hemolyzed, putting the infant at risk for severe hyperbilirubinemia[14].

Majority of neonates in this study were having blood group B+ followed by A+ with the frequencies of 37.5% and 31% respectively. The distribution of ABO blood group varies world-wide. Blood group O was the most common blood group found in one local study and other international studies except in Nepal where A was the most common (34%) and O was 1.5% less common (32.5%) than A[23-26]. With few exceptions ABO blood group distribution in various ethnic groups in one local study[27] was not significantly different from each other. While it was compared with earlier studies performed, by Majeed T et al[28] on 3000 subjects in Lahore, and by Bhatti FA[29] in Rawalpindi, blood group B was the most frequent (35.8%) blood group. In another local study[27] the authors found blood group B was the most frequent blood group in Arain (40.5%), and blood group O was less common (24.7%) while it was the most frequent blood group among Awans, Rajputs, miscellaneous Punjabi sub casts, Balochs, Sindhis, and Pathans that has not been documented in earlier studies, however it agreed with the study performed by Bhatti R[30] in Sindh on 38,000 subjects, and by Mian et al[31] in Multan on 1632 subjects. This difference may be due to difference of sample sizes of these studies and requires further comprehensive studies to confirm.

CONCLUSIONS

Out of 200 neonates presented with jaundice, frequency of ABO-incompatibility was found to be 22.5% followed by Rh-incompatibility 12.5%. Majority of neonates with jaundice presented on their first day of life with the frequency of 45%.

REFERENCES

1. Kliegman RM. Digestive system disorders: jaundice and hyperbilirubinemia in the newborn. In: Behrman RE, Kliegman RM, Jenson HB, editors. Nelson's textbook of pediatrics. 18th ed. New Delhi: Saunders, 2008.p.756-66.
2. Eneh AU, Ugwu RO. Perception of neonatal jaundice among women attending children out patient and immunization clinics of the UPTH Port Harcourt. Niger J Clin Pract 2009;12:187-91.
3. Shaheen R, Subhan F, Tahir F. Severe Rh-D alloimmunisation: a miraculous suppression of immunogenicity. Pak J Med Res 2005:44:133-5.

4. McIntosh N, Stenson B. The newborn. In: McIntosh N, Helms PJ, Symth RL, editors. Forfar & Arneil's textbook of pediatrics. 6th ed. Edinburgh: Churchill Livingstone, 2003.p.177-391.

5. Drabik-Clary K, Reddy VV, Benjamin WH, Boctor FN. Severe hemolytic disease of the newborn in a group B African-American infant delivered by a group O mother. Ann Clin Lab Sci 2006:36:205-7.

6. Waheed I, Chishti AL, Alvi A, Iqbal A. Hemolytic disease of newborn: Can we meet this challenge? Pak Paediatr J 2005;29:129-32.

7. Thilo EH, Rosenburg AA. The newborn infant: common problems in the newborn infant: neonatal jaundice. In: Hay WW, Levin MJ, Sondheimer JM, Deterding RR, (edi). Current pediatric diagnosis and treatment. 18th ed. New York: Lange Medical Books/McGraw-Hill, 2007.p.11-7.

8. Eder AF. Alloimmune hemolytic disease of the fetus and newborn. In: Greer JP, Foerster J, Lakens JN, Rodgers GM, Paraskevas F, Glader B, eds. Wintrobe's clinical hematology. 11th ed. Philadelphia: Lippincott Williams & Wilkins, 2004.p.1183-1202.

9. Bhutani VK, Johnson L. Prevention of severe neonatal hyperbilirubinemia in healthy infants of 35 or more weeks of gestation: implementation of a systems-based approach [Editorial]. J de Pediatria 2007;83:289-93.

10. Wikipedia, the free encyclopedia. Jandice. [Online] 2010 [Cited on 2010, April 10]. Available from: URL://http:// www.en/ wikipedia.org/wiki/jandice.htm

11. Skae MS, Moise J, Clarke P. Is current management of neonatal jaundice evidence based? Arch Dis Child Fetal Neonatal Ed 2005;90:F540.

12. Evans D. Neonatal jaundice. Clin Evid (Online) 2007;pii:0319.

13. Weng YH, Chiu YW. Spectrum and outcome analysis of marked neonatal hyperbilirubinemia with blood group incompatibility. Chang Gung Med J 2009;32: 400-7.

14. Moerschel SK, Cianciaruso LB, Tracy LR. A practical approach to neonatal jaundice. Am Fam Physician 2008;77:1255-62.

15. Khattak ID, Khan TM, Khan P, Shah SMA, Khattak ST, Ali A. Frequency of ABO and rhesus blood groups in district Swat, Pakistan. J Ayub Med Coll 2008;20:127-9.

16. Masood MK, Afridi IUK, Rizwan M, Yaqoob M, Izhar TS, Qureshi AW. Complications and immediate clinical outcome of exchange transfusion in Neonatal hyperbilirubinemia. Pak Paed J 2005;29:3-8.

17. Owa JA, Ogunlesi TA. Why we are still doing so many exchange blood transfusion for neonatal jaundice in Nigeria. World J Pediatr 2009;5:51-5.

18. Maisels MJ. Neonatal jaundice. Pediatr Rev 2006;27:443-54.

19. Cakmak A, Calik M, Atas A, Hirfanoglu I, Erel O. Can haptoglobin be an indicator for the early diagnosis of neonatal jaundice? J Clin Lab Anal 2008;22:409-14.

20. American Academy of Pediatrics Subcommittee on Hyperbilirubinemia. Management of hyperbilirubinemia in the newborn infant 35 or more weeks of gestation. Pediatrics 2004;114 :297-316.

21. Maisels MJ, Kring EA. Does intensive phototherapy produce hemolysis in newborns of 35 or more weeks gestation? J Perinatol 2006;26:498-500.

22. Maisels MJ, McDonagh AF. Phototherapy for neonatal jaundice. N Engl J Med 2008;358: 920-8.

23. Das PK, Nair SC, Harris VK, Rose D, Mammen JJ, Bose YN, et al. Distribution of ABO and RhD blood group among blood donors in a tertiary care center in South India. Trop Doct 2001;31:47-8.

24. Mwangi J. Blood group distribution in an urban population of patient targeted blood donors. East Afr Med J 1999;76:615-8.

25. Omotade OO, Adeyemo AA, Kayode CM, Falade SL, Ikpeme S. Gene frequencies of ABO and Rh (D) blood group alleles in a healthy infant population in Ibadan, Nigeria. West Afr J Med 1999;18:294-7.

26. Pramanik T, Pramanik S. Distribution of ABO and Rh blood groups in Nepalese medical students: a report. East Mediterr Health J 2000;6:156-8.

27. Ali N, Anwar M, Bhatti FA, Nadeem M, Nadeem A, Ali AM. Frequency of ABO and Rh blood groups major ethnic groups and casts of Pakistan. Pak J Med Sci 2005;21:26-9.

28. Majeed T, Hayee A. Prevalence of ABO blood groups and subgroups in a population of Lahore. Biomedica 2002;18:11-5.

29. Bhatti FA, Amin M. Spectrum of ABO and D blood groups of donors at Rawalpindi/ Islamabad. Pak J Pathol 1996;7:26-8.

30. Bhatti R. Frequency of ABO and Rh (D) Blood Groups in human population of southern Sindh (Pakistan). Ann King Edward Med Coll 1998;4:32-3.

31. Mian A, Farooq A. Distribution of ABO and RH blood group alleles in different populations of southern Punjab, Pakistan. Anthropol ANZ 1999;57:33-9.

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