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Frequency of ABO Incompatibility in Neonates as Cause of Neonatal Jaundice admitted in a Neonatal Unit of Tertiary Care Hospital

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ABSTRACT

Objective: To determine the frequency of maternal-fetal ABO incompatibility in newborns with neonatal jaundice.
Study Design: Cross-sectional study.
Place and Duration of Study: Neonatal Intensive Care Unit, Pak Emirates Military Hospital, Rawalpindi Pakistan from Apr 2020 to Jan 2021.
Methodology: All full-term newborns of either gender presenting with neonatal jaundice and need of phototherapy were consecutively enrolled. ABO blood incompatibility in neonatal jaundice was labelled as positive based on the presence of increased levels of serum indirect bilirubin in a newborn with blood group type A or B and maternal blood group type O. Information was collected regarding gender, birth weight, duration of hospital stay, hemoglobin level on admission, hematocrit level, indirect bilirubin level, direct Coombs test, duration of phototherapy, and need for intravenous immunoglobulin therapy.
Results: Of 225 neonates, the mean birth weight was 3283.12±1116.11 grams. The ABO incompatibility was observed in 37(16.4%) infants. The findings of multivariable analysis revealed that, after adjusting for other covariates, the odds of ABO incompatibility was 3.28 times higher among neonates with hemolysis as compared to the neonates without hemolysis (aOR 3.28, 95% CI 1.42-7.71). Similarly, after adjusting for other covariates, the odds of ABO incompatibility was 3.53 times higher among neonates with >50 hours of phototherapy duration as compared to neonates with ≤50 hours of phototherapy duration (aOR 3.53, 95% CI 1.40-8.89).
Conclusion: In conclusion, 16.4% newborns with neonatal jaundice were ABO incompatible. Moreover, hemolysis and longer phototherapy requirement were considerably higher in these neonates than those who were not ABO incompatible.

Keywords: ABO incompatibility, Blood group system, Indirect bilirubin, Jaundice.

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INTRODUCTION

Neonatal jaundice is one of the most frequent causes of fetal morbidity, accounting for about 10% to 35% of all hospital admissions.[1,2] Neonatal jaundice affects up to 80% of preterm and 60% of full-term neonates in their first week of life.[3] The said condition can cause encephalopathy and even death during this period.[4] One of the causes of neonatal jaundice is ABO incompatibility. Neonates affected by ABO incompatibility may experience hemolysis associated with jaundice within first 24 hour of neonatal life.[5] This may lead to mild anemia in rare cases. It is point of contention whether it is considered pathological or physiological condition, as physiological jaundice in infancy occurs in 2nd and 4th days of life. While with ABO incompatibility, jaundice appears in 24 hours indicating that it is pathological.[5] Mother with blood group O having fetus with blood group A or B may develop maternal-fetal ABO incompatibility. ABO incompatibility in these fetuses causes severe hyperbilirubinemia (serum bilirubin of >15 mg/dl). Serum bilirubin will usually not rise above 10 mg/dl in full term and 15mg/dl in preterm in physiological jaundice and disappears within 2 weeks of life.[6]

It is reported in literature that ABO incompatibility occurs in 15-20% of all pregnancies.[7] About 10% of ABO incompatible neonates experience hemolytic disorder, which is related to clinically severe neonatal jaundice.[8,9] In addition these infants exhibit severe anemia within first few months.

Maternal-fetal ABO incompatible newborns are at increased risk for developing significant hyperbilirubinemia, and therefore, prediction of probable risk factor, such as hemolysis, becomes important. The factors responsible for disparity in

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hospital stay, severity of jaundice and fall in hemoglobin levels in a newborn with neonatal jaundice can be explained by the degree of hemolysis associated with ABO incompatibility. Given the seriousness of the condition and its possible sequalae, and the dearth of similar studies in our region, our study aimed to determine the frequency and effects of maternal-fetal ABO in-compatibility in neonates.

METHODOLOGY

The cross-sectional study was conducted at Neonatal Intensive Care Unit of Pak Emirates Military Hospital, Rawalpindi Pakistan, from April 2020 to January 2021 after the approval from IERB (IERB #: A/28/208/2020). Utilizing EpiInfo calculator, with previously reported prevalence of ABO incompatibility 17.33%.[10]

Inclusion Criteria: Full-term newborns (those having a gestational age greater than 37 weeks) of either genders, diagnosed neonatal jaundice; neonates requiring phototherapy were included.

Exclusion Criteria: Neonates with any congenital abnormality; direct hyperbilirubinemia; neonatal sepsis; hypothyroidism were excluded.

All eligible neonates were enrolled through non-probability consecutive sampling. Signed informed consent was obtained from all eligible study participants before enrolment in the study.

Neonatal jaundice was defined as the presence of serum indirect bilirubin of >15 mg/dl.[10] Whereas ABO blood incompatibility in neonatal jaundice was considered positive based on the presence of increased level of total serum bilirubin in a newborn infant with blood type A or B and maternal blood type O.

Relevant examination was performed to diagnose the blood group of both neonates and mother. Information was collected regarding the demographic characteristics of the neonate like gender, birth weight, and duration of hospital stay. Furthermore, clinical and laboratory parameters like hemoglobin level on admission, hematocrit level, indirect bilirubin level, direct Coombs test, duration of phototherapy, and need for intravenous immunoglobulin (IVIG) therapy were observed.

Data was analyzed using Statistical Package for Social Sciences (SPSS) version 24. Mean±SD was calculated for quantitative variables. Moreover, frequencies and percentages were explored for qualitative variables. Chi-square test/Fisher's exact test was applied. Furthermore, independent t-test was also applied to see the mean difference of quantitative variables in between ABO incompatibility presence and absence. The *p*-value of ≤0.05 was considered as statistically significant. Lastly, binary logistic regression analysis was performed to determine predictors of associated with ABO incompatibility.

RESULTS

A total of 225 neonates were included in the study with female preponderance 115(51.1%). Mean birth weight was 3283.12±1116.11 gram (3.28kg). Mean duration of hospital stay was 4.85±2.62 days, with more than 5 days in 89(39.6%) neonates. Mean hemoglobin was 11.08±2.76 g/dL, with anemia being observed in 147(65.3%) of neonates. Elevated indirect bilirubin was observed in all infants with more than 22mg/dL in 162(72%) neonates. Direct Coombs teste was positive in 94(41.8%) cases, while 53(23.6%) cases showed hemolysis. IVIG was administered to 59(26.2%) neonates. (Table-I)

Table-I: Baseline Characteristics of the Patients (n=225)

Characteristics	n(%)
Gender	
Male	110(48.9)
Female	115(51.1)
Birth weight (grams)	3283.12±1116.11
≤3000	130(57.8)
>3000	95(42.2)
Duration of hospital stay (days)	4.85±2.62
≤5	136(60.4)
>5	89(39.6)
Initial Hb (gm/dL)	11.08±2.76
Anemic	147(41.8)
Non-anemic	78(34.7)
Initial HCT (%)	37.03±6.83
≤37	121(53.8)
>37	104(46.2)
Initial Indirect Bilirubin (mg/dL)	22.52±5.76
≤22	63(28.0)
>22	162(72.0)
Positive Direct Coombs Test	
Yes	94(41.8)
No	131(58.2)
Hemolysis	
Yes	53(23.6)
No	172(76.4)
Duration of phototherapy (hours)	50.32±18.89
≤50	171(76.0)
>50	54(24.0)
Need of IVIG Therapy	
Yes	59(26.2)
No	166(73.8)

The frequency of ABO incompatibility was observed in 37(16.4%) newborns with neonatal jaundice. There was a significant difference in the mean birth weight (*p*-value 0.003) and initial indirect bilirubin (*p*-value<0.001) amongst neonates with and without ABO incompatibility (Table-II). Moreover, the comparison of ABO incompatibility showed significant association with initial indirect bilirubin (*p*-value 0.011), anemia (*p*-value 0.028), hemolysis (*p*-value<0.001), and need of IVIG therapy (*p*-value 0.003). (Table-III)

Table-II: ABO Incompatibility of the Neonates (n=225)

Characteristics	ABO Incompatibility		*p*-value
	Mean±SD	Mean±SD	
Birth weight (grams)	2792.8±1084.1	3379.6±1099.5	0.003
Duration of hospital stay (days)	4.24±2.46	4.97±2.6	0.122
Initial Hb (gm/dL)	11.3±2.09	11.6±2.7	0.598
Initial HCT (%)	36.7±6.6	37.1±6.8	0.807
Initial Indirect Bilirubin (mg/dL)	26.1±2.7	22.5±5.8	<0.001
Duration of phototherapy (hours)	54.56±27.8	49.5±16.5	0.135

The findings of the univariate analysis revealed that the odds of ABO incompatibility were 2.62 times higher among neonates with ≤3000 g birth weight as compared to those with >3000 g birth weight (OR: 2.62, 95% CI: 1.17-5.86). The odds of ABO incompatibility were 2.36 times higher among neonates with positive direct Coombs test as compared to those with negative direct Coombs test (OR: 2.36, 95% CI: 1.15-4.85). The odds of ABO incompatibility were 2.60 times significantly higher among anemic neonates as compared to non-anemic neonates (OR:2.60, 95% CI: 1.08-6.23). The odds of ABO incompatibility were 2.95 times significantly higher among neonates who needed IVIG therapy as compared to those who did not need IVIG therapy (OR:2.95, 95% CI:1.42-6.14). Furthermore, the findings of the multivariable analysis revealed that after adjustment of other covariates, the odds of ABO incompatibility were 3.28 times higher among patients with hemolysis as compared to patients without hemolysis (aOR 3.28, 95% CI 1.42-7.71). After adjustment of other covariates, the odds of ABO incompatibility were 3.53 times higher among patients with >50 hours of duration of phototherapy as compared to the neonates with ≤50 hours of duration of phototherapy (aOR 3.53, 95% CI 1.40-8.89) (Table-IV).

Table-III: Comparison of ABO Incompatibility with Study Characteristics (n=225)

Parameters	ABO Incompatibility		p-value
	Yes (n=37)	No (n=188)	
Gender			
Male	19(17.3)	91(82.7)	0.743
Female	18(15.7)	97(84.3)	
Birth weight (grams)			
≤3000	28(21.5)	102(78.5)	0.016
>3000	9(9.5)	86(90.5)	
Duration of hospital stay (days)			
≤5	27(19.9)	109(80.1)	0.088
>5	10 (11.2)	79 (88.8)	
Initial HCT (%)			
≤37	19(15.7)	102(84.3)	0.746
>37	18 (17.3)	86 (82.7)	
Initial Indirect Bilirubin (mg/dL)			
≤22	4(6.3)	59(93.7)	0.011
>22	33 (20.4)	129 (79.6)	
Positive Direct Coombs Test			
Yes	22(23.4)	72(76.6)	0.017
No	15 (11.5)	116 (88.5)	
Anemia			
Yes	30(20.4)	117(79.6)	0.028
No	7(9.0)	71(91.0)	
Hemolysis			
Yes	17(32.1)	36(67.9)	<0.001
No	20(11.6)	152(88.4)	
Duration of phototherapy (hours)			
≤50	25(14.6)	146(85.4)	0.189
>50	12(22.2)	42(77.8)	
Need of IVIG Therapy			
Yes	17(28.8)	42(71.2)	0.003
No	20(12.0)	146(88.0)	

DISCUSSION

The current study was conducted at a large neonatal intensive care unit of a military hospital of Pakistan with the primary aim to assess the burden of ABO incompatibility among newborns with neonatal jaundice. For this purpose, term newborns with neonatal jaundice who needed of phototherapy were enrolled. The findings of the current study reported ABO incompatibility in almost sixteen percent of cases. The reported results of ABO incompatibility vary among different studies both nationally and internationally.[11,12,15] Abbas *et al*.[9] Ghaemi *et al*.[16] Hodr *et al*.[14] Cariani *et al*.[17] and Irshad *et al*.[18] has reported findings similar to our study. Other studies reported more lower percentage of neonatal ABO in-compatibility prevalence.[15,16]

Table-IV: Regression Analysis of Factors Associated with ABO Incompatibility (n=225)

Parameters	ABO Incompatibility			*p*-value
	OR (95% CI)	*p*-value	aOR (95% CI)	
Birth weight (grams)				
≤3000	2.62(1.17-5.86)	0.019	1.68 (0.65-4.28)	0.277
>3000	Ref		Ref	
Duration of hospital stay (days)				
≤5	1.95 (0.89-4.27)	0.092	1.64 (0.69-3.83)	0.257
>5	Ref		Ref	
Positive Direct Coombs Test				
Yes	2.36 (1.15-4.85)	0.019	1.92 (0.81-4.52)	0.138
No	Ref		Ref	
Anemia				
Yes	2.60(1.08-6.23)	0.032	2.16 (0.82-5.67)	0.118
No	Ref		Ref	
Hemolysis				
Yes	3.58(1.71-7.53)	0.001	3.28 (1.42-7.71)	0.005
No	Ref		Ref	
Duration of phototherapy (hours)				
>50	1.67(0.77-3.60)	0.192	3.53 (1.40-8.89)	0.007
≤50	Ref		Ref	
Need of IVIG Therapy				
Yes	2.95(1.42-6.14)	0.004	2.34 (0.96-5.64)	0.060
No	Ref		Ref	

In the current research, serum bilirubin level and hemoglobin level were considerably higher in neonates with ABO incompatibility. In concurrence with our study, Akgul *et al*.[8] and Shah *et al*.[19] reported considerably higher level of serum bilirubin and hemoglobin level in neonates with ABO incompatibility. It is reported that serum bilirubin levels were elevated gradually and reach to dangerous levels after birth for neonates suffering from hemolytic disease due to ABO incompatibility,[20] which is in line with our findings.

In the present study, ABO incompatible neonates with hyperbilirubinemia required phototherapy (>50 hours) more than three times higher than those who had ABO compatibility which was also reflected in a study that reported 30.4% of ABO-incompatible newborns had significant hyperbilirubinemia and required phototherapy for 44-68.1 hours.[21]

According to the current study findings, ABO incompatibility was also found considerably higher in neonates with hemolysis than that of those without hemolysis. It is reported in literature that blood group should be evaluated as early as possible for all neonates with maternal blood group of O, since there is increased risk of developing hyperbilirubinemia and or hemolytic disease in neonates due to incompatible ABO blood system.[9]

LIMITATION OF STUDY

Inability to detect and compare the different causes of neonatal hyperbilirubinemia was limitation of this study. Moreover, as this study was conducted during CoronaVirus-19 (COVID-19) disease pandemic, the collection of the sample was a challenge. Due to the difficulties faced during the pandemic, certain important predictor variables were not studied.

CONCLUSION

In conclusion, 16.4% newborns with neonatal jaundice were ABO incompatible. Moreover, hemolysis and longer phototherapy requirement were considerably higher in these neonates. Maternal-fetal blood group screening and early management in case of ABO incompatibility would be effective in reducing neonatal jaundice complications.

Conflict of Interest: None.

Authors Contribution

Following authors have made substantial contributions to the manuscript as under:

AJ & FI: Conception, study design, drafting the manuscript, approval of the final version to be published.

RN & SM: Data acquisition, data analysis, data interpretation, critical review, approval of the final version to be published.

MH & SA: Data acquisition, drafting the manuscript, approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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