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FREQUENCY OF ABO INCOMPATIBILITY IN NEONATAL JAUNDICE

Sanam[*1], Mahesh Kumar[2], Ghulam Rasool Bouk[3]

[*1,2,3]*Ghulam Muhammad Mahar Medical College (GMMMC), Sukkur*

[*1]sanmairakhan15@gmail.com, [2]Maheshkumarathwani@gmail.com, [3]gr.bouk@gmail.com

Corresponding Author: *
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ABSTRACT

BACKGROUND: *Neonatal jaundice is a relatively common phenomenon, which is frequently associated with the condition of the newborn, having hemolysis from the incompatibility of maternal antibodies with the fetal red blood cells, and ABO blood groups. Such incompatibility is especially prevalent in areas with high rates of consanguinity including Pakistan. It is imperative to know its prevalence in jaundiced neonates to facilitate early diagnosis and management, which in turn will minimize complications and improve neonatal outcome in resource-constrained settings.*

METHODOLOGY: *This prospective descriptive study was conducted at Ghulam Muhammad Ali Mahar Medical College Teaching Hospital and 174 full-term (0–28 days) neonates were included in the study by non-probability consecutive sampling. ABO incompatibility was assessed through comparison of maternal and neonatal blood groups in neonates diagnosed with jaundice (bilirubin >15 mg/dL). Data were analyzed using SPSS 26.0*

RESULTS: *ABO incompatibility was found in 16.3% of jaundiced neonates, with 49% males and 51% females, and a mean age of 13.3 ± 8 days. It was significantly associated with anemia (22.4%, OR 6.8), elevated bilirubin levels (>22 µmol/L, OR 0.26), positive Coombs tests (24.1%, OR 2.5), hemolysis (31.4%, OR 3.5) and IVIG therapy was found to be in (28.6%, OR 3.1) cases.*

CONCLUSION: *It is to be concluded that ABO incompatibility is an important cause of jaundice in a neonate with a higher risk of anemia, hemolysis, and hyperbilirubinemia requiring an intensive therapy line, such as IVIG therapy. Within this already vulnerable subgroup of patients, early detection and treatment, such as with phototherapy and occasionally also exchange transfusions, is crucial for minimising sequelae and for improving neonatal outcome.*

Keywords: *ABO Incompatibility, Neonatal Jaundice, Newborn, Hyperbilirubinemia*

INTRODUCTION

Neonatal jaundice is a common neonatal disorder that affects around 60% of term and 80% of preterm infants in the first week of life [1]. It appears as a yellow discoloration of the skin and sclera due to high levels of bilirubin in the bloodstream. While most cases of jaundice in the neonate are benign and self-limiting, severe degrees of hyperbilirubinemia give rise to acute bilirubin encephalopathy and kernicterus, the sequelae of which are permanent neurological disability and even death [2,3]. The risk for these serious complications is therefore why early recognition and treatment of the underlying causes of neonatal jaundice is so important. ABO blood group incompatibility is an important, well-known cause of neonatal jaundice

among multiple etiologies. This happens when an antibody of an A or B mother and the mother has blood group O blood group or when the child has A or B blood group. This incompatibility results in lysis of the neonate's red blood cells, as maternal IgG antibodies cross the placenta and destroy the red blood cells of the neonate, with excess bilirubin production as a consequence [4]. This hemolysis results in considerable hyperbilirubinememia, complicated by medical intervention. The frequency of ABO blood group incompatibility in jaundiced neonates differs widely among populations and studies. Ilyas et al. ABO incompatibility was identified in 26.4% of jaundiced neonates admitted [5]. However, prevalence of 12% was similarly reported by Thakur S, et al in 2020 [6]. An examination conducted recently by Jamil A et al [13] even reported that ABO incompatibility accounted for 16.4% of neonates with jaundice, thus maintaining importance in pathogenesis of neonatal jaundice. The implications of these findings are significant; early diagnosis and therapy of this condition is vital in preventing severe, complicated hyperbilirubinemia. Despite improvements in diagnosis and therapeutics, we need more epidemiologic studies in order to better understand the consequences of ABO incompatibility in jaundiced neonates. With the currently available diagnostic techniques, including the direct antiglobulin test (DAT) and transcutaneous bilirubinometry, the diagnosis of this condition is more reliable [7–8]. Ultimately, phototherapy and even exchange transfusion in extreme occasions are nevertheless vitals in treating hyperbilirubinemia in neonates with ABO incompatibility [9--10]. Neonatal jaundice is one of the most common and significant health problems in Pakistan because of its high prevalence and complications [11-12]. ABO blood group incompatibility which is one of the major causes of neonatal jaundice is found highly prevalent in Pakistan due to heterogenetic nature of mankind as well as more frequent consanguineous marriages. Management of these cases can lead to improved outcomes, however local data to inform best practices is limited. The purpose of this study was to ascertain the frequency of ABO incompatibility among symptomatic jaundiced newborns and to suggest possible modifications to current screening and treatment algorithms.

METHODOLOGY

This research was conducted at the Outpatients Department of Ghulam Muhammad Ali Mahar Medical College Teaching Hospital and included 174 neonates selected through non-probability consecutive sampling. Participants were neonates aged 0–28 days, of either gender, born full-term with a gestational age of at least 37 weeks, verified by the mother's last menstrual period (LMP). Only neonates diagnosed with jaundice were included in the study. Jaundice was characterized as a yellow discoloration of the skin and sclera, visible under natural light, starting from the head and moving downward, with serum indirect bilirubin levels exceeding 15 mg/dL. The focus of the study was to identify ABO incompatibility by comparing the blood groups of mothers and their neonates. ABO incompatibility was defined as cases where mothers with blood group O+ve had neonates with blood groups A+ve, B+ve, A-ve, or B-ve, or mothers with blood group O-ve had neonates with blood groups A-ve or B-ve. This condition occurs when antibodies produced by the mother against fetal red blood cells cross the placenta, causing hemolysis and leading to jaundice in the neonate.

Exclusion criteria encompassed neonates with physiological jaundice, concurrent ABO and Rh incompatibility, direct hyperbilirubinemia (direct bilirubin >20% of total), congenital anomalies, neonatal sepsis, hypothyroidism, significant bruising, cephalohematoma, or those who had undergone exchange transfusion prior to enrollment. Data collection commenced with informed consent from the parents or guardians, who were provided with detailed information about the study. Information such as the neonate's age, gender, weight, hemoglobin levels, hematocrit, and bilirubin levels were recorded on a structured proforma. Blood samples from both neonates and their mothers were analyzed in the hospital laboratory to confirm the presence of ABO incompatibility. The SPSS version 26.0 was used to analyze statistical data. Descriptive statistics were summarized in terms of mean with standard deviation and frequency with percentage. The Chi-square test was applied to assess the statistical significance at 5% level of significance.

RESULTS

There were 147 study participants with a mean age of 13.29 ± 8.04 days, of which 59.2% were ≤ 13 days old and 40.8% were > 13 days old. Birth weight had a mean of 3107.68 ± 704.88 g (68.7% from 1500–3000 g and 31.3% more than 3000 g), and duration of hospital stay had a mean of 4.62 ± 1.76 days (66.7% from 2–5 days and 33.3% more than 5 days). The mean value of initial hemoglobin was 10.42 ± 1.12 g/dL, and 66.7% included in the anemic group and 33.3% in the non-anemic group. The mean initial level of hematocrit was 33.71 ± 6.14%, with 56.5% having levels between 25–37% and 43.5% having levels >37%. The mean value of the first indirect bilirubin was 24.32 ± 5.83 µmol/L, where 32.0% of patients had values in the range of 17-22 µmol/L and 68.0% >22 µmol/L; the mean time of phototherapy was 49.81 ± 9.28 hours, where 74.1% underwent phototherapy for 24-50 hours and 25.9% >50 hours. Of the cohort, 49.0% males, and 51.0% females. The direct Coombs test was found to be positive in 39.5% of cases and negative in 60.5% of cases. Amongst all participants, hemolysis was noted in 23.8% of cases, while IVIG therapy was required in 28.6%—and not required in 71.4% as shown in **TABLE I**.

Patient characteristics included in the study are listed in **Table II** comparing 24 patients with ABO incompatibility to 123 without. The proportion of patients with ABO incompatibility born with a birth weight of 1500–3000 g was significantly greater compared to those born weighing >3000 g (OR 3.762, 95% CI: 1.062–13.334, p=0.022). ABO incompatibility was much more prevalent among anemic patients (22.4%) than non-anemic patients (4.1%) with an OR of 6.803 (95%CI:1.529–30.260, p=0.003). ABO incompatibility was found in 21.0% of patients with initial indirect bilirubin levels >22 µmol/L and in 6.4% of patients with levels between 17–22 µmol/L (OR = 0.256 (95% CI: 0.072–0.908, p=0.018)). Patients with ABO incompatibility had more often a positive direct Coombs test (24.1% versus 11.2%) (OR 2.514, 95% CI: 1.031–6.129, p=0.039) Compared to patients without ABO incompatibility, hemolysis was also more common in those with ABO incompatibility (31.4% vs. 11.6%, OR: 3.490, 95% CI: 1.393–8.745, p=0.006). Furthermore, the patients with ABO incompatibility had higher rate of need for IVIG therapy (28.6%) than that without (11.4%) (OR: 3.100, 95% CI: 1.261–7.623, p=0.011). Age group, duration of hospital stays, initial hematocrit level, duration of phototherapy and gender did not make any significant difference.

DISCUSSION

ABO incompatibility is an important reason for neonatal jaundice, which is mainly due to hemolysis from maternal and child blood type interaction. This situation occurs when the blood group of mothers is O type so that she has produced IGM antibodies against the A or B antigens of the child, and those IgG antibodies can cross the placenta and cause hemolysis of fetal red blood cells after birth [14]. The hemolysis leads to an increase in non -conjugated bilirubin which results in jaundice and bilirubin encephalopathy if not adequately treated.

ABO incompatibility can lead to a wide range of clinical manifestations, from mild hyperbilirubinemia to more serious life-threatening forms requiring urgent treatment [15]. Maternal serum bilirubin level, time of initiation and coexistent conditions affect the severity of jaundice [16]. The high burden of neonatal jaundice in settings with high prevalence of ABO incompatibility as reported from Ethiopia makes it an important public health problem [17].

In case of incompatibility of ABO, bilirubin is closely monitored and once it crosses the exchange transfusion threshold, phototherapy is the primary mode of treatment [18]. In severe cases, exchange transfusions will be required to rapidly lowered bilirubin levels [19]. The identification of mother-child pairs at risk during prenatal visits, through blood grouping and maternal antibody titration are the prevention measures. Regular screening can also assist in secondary prevention by reducing adverse impact on the health of infants [20,21].

Considering the incompatibility of ABO is an important cause of newborn and infant health problems, effective management and prevention strategies are essential to reduce its burden; however, neonatal fototherapy and other risk factors should be diagnosed and treated in a timely manner minimizing associated harms.

ABO incompatibility was found in 16.32% in our study. In another study ABO incompatibility in neonates was seen in 26.4% [5] of cases while in a study conducted by Thakur S, et al it was 12% [6]. In a study done by Jamil A, et al, ABO incompatibility was found to be 16.4% [13]. An incidence of 17.33% was documented by Abbas SH et al [21].

ABO incompatibility: Early recognition and management of ABO incompatibility is one of the strengths of this condition in neonatal jaundice. Also, this condition is quite common and has a well understood pathophysiology so it is more easy to diagnose and follow. The jaundice is expected with the bilirubin levels generally rising in the first 24 hours of life. In addition, jaundice due to ABO incompatibility is also generally regarded as amenable to treatment. The most widely used treatment is phototherapy, which works by chemicals in the baby's skin breaking down the bilirubin. In severe cases, exchange transfusions may be necessary, but these are rare these days because of the availability of phototherapy.

The easy and immediate availability of blood group reports can help clinicians in managing ABO incompatibility but there are still some weaknesses or challenges in this regard. While being the most common cause of jaundice in neonates, the disorder can still have life-threatening complications if not recognised or treated in time. Sometimes, the jaundice becomes worse very quickly, and if not treated in time, this can cause kernicterus — bilirubin-induced brain damage. Also, where the treatment schedule should be carefully balanced and excessive treatment will lead to hazardous interventions while insufficient treatment will increase the complications. Significance Bilirubin levels are closely monitored in the early few days of life, especially in at-risk infants.

This is another challenge to overcame for the treatment of ABO incompatibility in cases of jaundice condition. Although most cases will be treatable with phototherapy, some infants require more intensive interventions like exchange transfusions to avoid complications. Such interventions are resource- and personnel-intensive. Further, infants who develop more severe phototherapy resistant jaundice remain difficult to identify. We do not have currently a well-validated tool to identify the high-risk neonate, but development of predictive models or biomarkers might help in the early identification of such infants in the future.

As for the recommendations, screening and monitoring of the bilirubin levels should be performed early on, especially in the newborn with a risk for ABO incompatibility. Identifying infants at risk allows for timely intervention, reducing the likelihood of severe sequelae. Improved risk stratification tools that incorporate gestational age and weight along with ABO incompatibility could also facilitate better outcomes. Finally, health systems should prepare the clinicians who interpret these test results and assess and manage the downstream effects, including the complexities associated with ABO incompatibility. Additionally, although phototherapy is a mainstay of therapy, it would be nice to get more studies on the new modalities, such as the pharmacologicals that exist or the combination strategies. Wider parental education on the early detection of jaundice and the need for timely treatment may also be important in reducing the severity of the disease.

CONCLUSION

It is to be concluded that ABO incompatibility is an important cause of jaundice in a neonate with a higher risk of anemia, hemolysis, and hyperbilirubinemia requiring an intensive therapy line, such as IVIG therapy. Within this already vulnerable subgroup of patients, early detection and treatment, such as with phototherapy and occasionally also exchange transfusions, is crucial for minimising sequelae and for improving neonatal outcome.

Table I: Characteristics of Study Participants (n=147)	
Variable	**n (%)**
Age (Mean ± SD) = 13.29 ± 8.04	
0 - 13 days	87 (59.2)
>13 days	60 (40.8)
Birth Weight (Mean ± SD) = 3107.68 ± 704.88	
1500 - 3000 gm	101 (68.7)
>3000 gm	46 (31.3)
Duration of Hospital Stay (Mean ± SD) = 4.62 ± 1.76	
2 - 5 days	98 (66.7)
>5 days	49 (33.3)
Initial Hemoglobin Level (Mean ± SD) = 10.42 ± 1.12	
Anemic	98 (66.7)
Non-Anemic	49 (33.3)
Initial Hematocrit Level (Mean ± SD) = 33.71 ± 6.14	
25 - 37 %	83 (56.5)
>37 %	64 (43.5)
Initial Indirect Bilirubin (Mean ± SD) = 24.32 ± 5.83	
17 - 22 µmol/L	47 (32.0)
>22 µmol/L	100 (68.0)
Duration of Phototherapy (Mean ± SD) = 49.81 ± 9.28	
24 - 50 hours	109 (74.1)
>50 hours	38 (25.9)
Gender	
Male	72 (49.0)
Female	75 (51.0)
Positive Direct Coombs Test	
Yes	58 (39.5)
No	89 (60.5)
Hemolysis	
Yes	35 (23.8)
No	112 (76.2)
Need of IVIG Therapy	
Yes	42 (28.6)
No	105 (71.4)

Table II: Characteristics of Patients with ABO Incompatibility (n=147)					
Variables		**ABO Incompatibility**		**OR 95% C. I**	**P-Value**
		Yes (n=24)	**No (n=123)**		
Age Group	0 - 13 days, *n* (%)	12 (13.8)	75 (86.2)	0.640 (0.266----1.540)	0.317
	>13 days, *n* (%)	12 (20.0)	48 (80.0)		
Birth Weight	1500 - 3000 gm, *n* (%)	21 (20.8)	80 (79.2)	3.762 (1.062----13.334)	0.022*
	>3000 gm, *n* (%)	3 (6.5)	43 (93.5)		
Duration of Hospital Stay	2 - 5 days, *n* (%)	19 (19.4)	79 (80.6)	2.116 (0.739----6.059)	0.156
	>5 days, *n* (%)	5 (10.2)	44 (89.8)		
Initial Hb Level	Anemic, *n* (%)	22 (22.4)	76 (77.6)	6.803 (1.529----30.260)	0.003*
	Non-Anemic, *n* (%)	2 (4.1)	47 (95.9)		
Initial HCT	25 - 37 %, *n* (%)	12 (14.5)	71 (85.5)	0.732 (0.305----1.760)	0.485
	>37 %, *n* (%)	12 (18.8)	52 (81.3)		
Initial Indirect Bilirubin	17 - 22 µmol/L, *n* (%)	3 (6.4)	44 (93.6)	0.256 (0.072----0.908)	0.018*
	>22 µmol/L, *n* (%)	21 (21.0)	79 (79.0)		
Duration of Phototherapy	24 - 50 hours, *n* (%)	15 (13.8)	94 (86.2)	0.514 (0.204----1.297)	0.154
	>50 hours, *n* (%)	9 (23.7)	29 (76.3)		
Gender	Male, *n* (%)	13 (18.1)	59 (81.9)	1.282 (0.533----3.083)	0.578
	Female, *n* (%)	11 (14.7)	64 (85.3)		
Positive Direct Coombs Test	Yes, *n* (%)	14 (24.1)	44 (75.9)	2.514 (1.031----6.129)	0.039*
	No, *n* (%)	10 (11.2)	79 (88.8)		
Hemolysis	Yes, *n* (%)	11 (31.4)	24 (68.6)	3.490 (1.393----8.745)	0.006*
	No, *n* (%)	13 (11.6)	99 (88.4)		
Need of IVIG Therapy	Yes, *n* (%)	12 (28.6)	30 (71.4)	3.100 (1.261----7.623)	0.011*
	No, *n* (%)	12 (11.4)	93 (88.6)		

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