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ORIGINAL ARTICLE

Outcome of Neonatal Jaundice in Term Neonates with ABO Blood group Incompatibility Admitted to the Special Care Baby Unit of Khyber Teaching Hospital

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ABSTRACT

Background: Neonatal jaundice is a common condition affecting newborns worldwide, with more than 50% of term and up to 80% of preterm infants developing hyperbilirubinemia. Although most cases are physiological, ABO blood group incompatibility is an important pathological cause resulting from maternal anti-A or anti-B antibodies crossing the placenta and causing hemolysis of fetal red blood cells. Affected neonates may develop early-onset jaundice, anemia, reticulocytosis, and severe hyperbilirubinemia, which can lead to bilirubin encephalopathy if not treated promptly. This study was conducted to evaluate the clinical outcomes, treatment interventions, and complications among term neonates with ABO incompatibility admitted to Khyber Teaching Hospital.

Methods: This descriptive study was conducted in the Department of Pediatric Medicine, Khyber Teaching Hospital, Peshawar from March 2026 to June 2026. A total of 210 term neonates with confirmed ABO incompatibility were included. Demographic details, laboratory parameters including total serum bilirubin, hemoglobin, reticulocyte count, and direct antiglobulin test (DAT), treatment modalities, complications, and duration of hospital stay were recorded and analyzed.

Results: Phototherapy was required in 150 (71%) neonates, intravenous immunoglobulin (IVIG) was administered to 45 (21%), and exchange transfusion was performed in 20 (9%). Anemia developed in 30 (14%) neonates, while bilirubin encephalopathy occurred in 5 (2%). Inferential analysis demonstrated that DAT-positive neonates were significantly more likely to require IVIG and exchange transfusion and had significantly longer hospital stays than DAT-negative neonates ($p < 0.05$).

Conclusion: ABO incompatibility remains a significant cause of neonatal jaundice among term infants. Early diagnosis, close monitoring, and timely therapeutic interventions are essential to prevent severe hyperbilirubinemia and associated complications.

Keywords: ABO incompatibility, Exchange Transfusion, Hyperbilirubinemia, Intravenous Immunoglobulin, Neonatal Jaundice, Phototherapy

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Introduction

Neonatal jaundice, defined as yellow discoloration of the skin and sclera resulting from elevated serum bilirubin levels, is one of the most common clinical conditions encountered during the neonatal period. More than half of term neonates develop some degree of jaundice during the first week of life, and although most cases are physiological, a significant proportion require medical evaluation and treatment (1, 2).

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Pathological jaundice may occur secondary to hemolytic diseases, infections, metabolic disorders, endocrine abnormalities, or hepatic dysfunction. The causes of hemolysis include ABO blood group incompatibility, a common and important condition in term neonates (3, 4).

ABO incompatibility occurs when a mother with blood group O has a neonate with blood group A or B. Maternal IgG antibodies cross the placenta and bind to fetal red blood cells leading to immune-mediated hemolysis (5, 6). The increased destruction of erythrocytes leads to increased bilirubin production and if not detected early may present as early-onset jaundice, anemia, reticulocytosis, and severe hyperbilirubinemia (4, 7). In severe cases, bilirubin toxicity may lead to bilirubin encephalopathy and permanent neurological sequelae (8).

Globally, ABO incompatibility is observed in approximately 20–25% of pregnancies; however, only a minority of affected neonates develop clinically significant hemolytic disease requiring treatment (6, 9). Nevertheless, ABO incompatibility remains an important cause of neonatal hyperbilirubinemia and hospital admission in many countries. Recent studies have reported that affected neonates frequently require phototherapy and, in selected cases, intravenous immunoglobulin (IVIG) or exchange transfusion(10,11,12,13). Diagnosis of ABO incompatibility is confirmed by blood group testing, clinical assessment, laboratory testing and Direct Antiglobulin Test (DAT). The presence of DAT, hyperbilirubinaemia, anaemia and reticulocytosis may be indicative of ongoing haemolysis and more severe disease (14, 15). Early detection of high risk neonates is especially important given the potential of early intervention to reduce the risk of severe hyperbilirubinaemia and its associated complications (16). Phototherapy is the mainstay of treatment of neonatal hyperbilirubinaemia and is effective in lowering serum bilirubin levels in most neonates (11, 17). Intravenous immunoglobulin is recommended in selected neonates with immune mediated haemolysis with rapidly rising bilirubin levels despite intensive phototherapy (12). Exchange transfusion is still reserved for severe cases with extreme hyperbilirubinemia or signs of acute bilirubin encephalopathy (13, 18).

Multiple studies have evaluated clinical features and outcomes of neonates with ABO incompatibility, but variations in treatment requirements, complications and hospital stay are still being reported (15, 19). ABO incompatibility is an important etiological factor for hospitalizations due to neonatal hyperbilirubinemia in Pakistan with a frequency of 18% - 28% reported in jaundiced neonates (9, 10). Similar findings have been reported from the tertiary care hospitals of Khyber Pakhtunkhwa where ABO incompatibility has been identified as a common cause of hemolytic neonatal jaundice requiring phototherapy and in some cases, exchange transfusion (10). Although neonatal jaundice is a common clinical condition leading to admissions in this part of the world, there is dearth of published data on clinical outcomes, treatment needs and complications among term neonates with ABO incompatibility.

Therefore, this study was conducted to evaluate the clinical outcomes, interventions and complications among term neonates with

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ABO blood group incompatibility admitted to the Department of Pediatric Medicine, Khyber Teaching Hospital. The findings of this study may help in better understanding of disease patterns and support evidence-based management of neonatal jaundice in healthcare settings with limited resources.

Methods

A hospital-based descriptive cross-sectional study was conducted at the Special Care Baby Unit (SCBU), Khyber Teaching Hospital, Peshawar, from March 2026 to June 2026. Ethical approval was obtained from the Institutional Research and Ethical Review Board (IREB), Khyber Medical College/Khyber Teaching Hospital, Peshawar (Approval No. 733/DME/KMC; dated 18 July 2025). The study was designed to evaluate the clinical outcomes, treatment interventions, and complications among term neonates diagnosed with neonatal jaundice secondary to ABO blood group incompatibility. The sample size was calculated using OpenEpi software (Version 3.01) with a 95% confidence level, an anticipated frequency of hyperbilirubinemia among jaundiced neonates of 22.0%, and a margin of error of 5%. The minimum required sample size was calculated to be 210 term neonates.

A total of 210 term neonates with confirmed ABO incompatibility were included in the study using a non-probability consecutive sampling technique. The eligibility criteria for the study were neonates admitted to the hospital between 37 and 42 completed weeks of gestation with neonatal jaundice. Both DAT-positive and DAT-negative neonates with confirmed ABO incompatibility were included in the study. Neonates with other causes of pathological jaundice such as Rh incompatibility, G6PD deficiency, neonatal sepsis, cephalohematoma, congenital ano-malies, metabolic disorders or incomplete medical records were excluded from the study. Preterm neonates and neonates whose mothers received intrauterine transfusion or immunoglobulin therapy during pregnancy were also excluded. Neonatal jaundice was diagnosed clinically by yellow discoloration of the skin and sclera and confirmed by the measurement of total serum bilirubin (TSB). ABO incompatibility was defined as maternal blood group O with neonatal blood group A or B regardless of Direct Antiglobulin Test (DAT) status. Severe hyperbilirubinemia was defined according to the 2022 American Academy of Pediatrics (AAP) Clinical Practice Guideline as the serum bilirubin levels reaching the threshold for exchange transfusion according to postnatal age and gestational age. Anemia was defined as a hemoglobin concentration of <13 g/dL in term neonates, while reticulocytosis was defined as a reticulocyte count >5%.

Demographic and clinical details were recorded on a structured proforma after enrollment. The variables collected included gender, gestational age, birth weight, mode of delivery, age at onset of jaundice, laboratory parameters, treatment interventions, complications and duration of hospital stay. Laboratory investigations included total serum bilirubin (TSB), hemoglobin level, reticulocyte count and direct antiglobulin test (DAT) results. These data were retrieved from patient records and hospital laboratory reports. Treatment interventions were recorded for all enrolled neonates. Information regarding initiation and duration of phototherapy, administration of intravenous immunoglobulin (IVIG), repeat IVIG dosing, and performance of exchange transfusion was documented. Phototherapy and exchange transfusion were initiated according to the 2022 American Academy of Pediatrics (AAP) Clinical Practice Guideline for the Management of Hyperbilirubinemia in the Newborn Infant 35 or More Weeks of Gestation. Exchange

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transfusion was performed in neonates whose bilirubin level reached the age-specific exchange transfusion threshold or who developed clinical features suggestive of acute bilirubin encephalopathy despite intensive phototherapy, according to the 2022 AAP guideline. (20)

Clinical outcome variables included development of anemia, bilirubin encephalopathy and length of stay in hospital Neonates were monitored as per routine protocols of SCBU and all interventions were performed by qualified health care professionals as per institutional guidelines Data entry and statistical analysis was done using SPSS version 26 (IBM Corp., Armonk, NY, USA) Continuous variables were expressed as mean ± standard deviation and categorical variables were presented as frequencies and percentages. The Chi-square test was used to compare categorical variables, while the independent samples t-test was applied to compare continuous variables between two groups. A p-value <0.05 was considered statistically significant.

Results

The mean gestational age was 38.5 ± 1.2 weeks and the mean birth weight was 3050 ± 400 g. The method of delivery was vaginal in 60% of the births and cesarean section in 40%. The demographic characteristics are summarized in **Table 1**.

Table 1: Neonatal demographics

Parameter	Frequency/ Mean ± SD
Total Neonates	210
Male	112 (53%)
Female	98 (47%)
Gestational Age (Weeks)	38.5 ± 1.2
Mean Birth Weight (grams)	3050 ± 400
Vaginal Delivery	126 (60%)
Cesarean Delivery	84 (40%)

The mean age at onset of jaundice was 36 ± 12 hours. The mean peak total serum bilirubin (TSB) level was 18.5 ± 3.5 mg/dL, while the mean hemoglobin level was 14.0 ± 1.8 g/dL. Direct antiglobulin test (DAT) positivity was observed in 74 (35%) neonates, and reticulocytosis (>5%) was present in 88 (42%) cases. The biochemical and laboratory characteristics are presented in **Table 2**.

Table 2. Clinical and Laboratory Findings

Parameter	Value
Age at Jaundice Onset (hours)	36 ± 12
Peak TSB (mg/dL)	18.5 ± 3.5
DAT Positive	74 (35%)
Hemoglobin (g/dL)	14 ± 1.8
Reticulocytosis (>5%)	88 (42%)

A total of 150 (71%) neonates required phototherapy, 45 (21%) received intravenous immunoglobulin (IVIG), and 20 (9%) underwent exchange transfusion. Inferential analysis demonstrated that DAT-positive neonates were significantly more likely to require phototherapy, IVIG administration, and exchange transfusion than DAT-negative neonates. DAT positivity was also significantly associated with anemia and reticulocytosis (all **$p < 0.05$**). These associations are presented in **Table 3**.

Table 3. Association of Direct Antiglobulin Test (DAT) Positivity with Treatment Interventions and Clinical Outcomes

Variable	DAT Positive (n = 74)	DAT Negative (n = 136)	p-value
Phototherapy	64 (86.5%)	86 (63.2%)	<0.001
IVIG	37 (50.0%)	8 (5.9%)	<0.001
Exchange transfusion	14 (18.9%)	6 (4.4%)	0.001
Anemia	21 (28.4%)	9 (6.6%)	<0.001
Reticulocytosis (>5%)	49 (66.2%)	34 (25.0%)	<0.001

Chi-square test was applied. A p-value of <0.05 was considered statistically significant.

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DAT-positive neonates had significantly higher peak total serum bilirubin levels than DAT-negative neonates (20.67 ± 4.32 mg/dL vs 17.25 ± 3.61 mg/dL, p < 0.001). Likewise, neonates who received IVIG and/or exchange transfusion had a significantly longer hospital stay than those managed without these interventions (6.03 ± 0.68 days vs 3.70 ± 0.70 days, p < 0.001), as shown in Table 4.

Table 4. Comparison of Peak Serum Bilirubin and Hospital Stay According to Clinical groups

Variable	Group	Mean ± SD	p-value
Peak total serum bilirubin (mg/dL)	DAT Positive (n = 74)	**20.67 ± 4.32**	**<0.001**
	DAT Negative (n = 136)	**17.25 ± 3.61**	
Hospital stay (days)	IVIG and/or Exchange transfusion (n = 49)	**6.03 ± 0.68**	**<0.001**
	No IVIG/Exchange transfusion (n = 161)	**3.70 ± 0.70**	

Values are presented as mean ± standard deviation. Comparisons were performed using the independent samples *t*-test. A p-value <0.05 was considered statistically significant.

Discussion

ABO incompatibility continues to be a clinically significant cause of neonatal jaundice and remains an important reason for neonatal admissions in many tertiary care hospitals. The present study evaluated the outcomes of term neonates with ABO incompatibility and demonstrated that a considerable proportion required therapeutic intervention during hospitalization. Most neonates were successfully managed with phototherapy, while a smaller proportion required IVIG or exchange transfusion. These findings are consistent with previous studies reporting that ABO incompatibility remains one of the most common causes of immune-mediated neonatal hyperbilirubinemia requiring hospital-based management (4, 6, 9). The underlying mechanism involves transplacental passage of maternal IgG anti-A and anti-B antibodies, which bind to neonatal erythrocytes and initiate hemolysis, resulting in excessive bilirubin production (5, 6). Consequently, although many affected neonates experience mild disease, a subset develops clinically significant hyperbilirubinemia requiring intensive treatment (7, 15).

In the present study, phototherapy was the most commonly used modality of treatment, required in more than two-thirds of neonates. This observation is not surprising as phototherapy is still the first-line treatment for neonatal hyperbilirubinemia and is very effective in reducing serum bilirubin levels (16, 17). Phototherapy converts the unconjugated bilirubin into water-soluble photoisomers that are excreted without hepatic conjugation, leading to rapid decline in serum bilirubin concentrations (16). The relatively high utilization of phototherapy in this study reflects the burden of hemolytic jaundice due to ABO incompatibility and the need for early treatment to prevent progression to severe hyperbilirubinemia. Similar rates of phototherapy utilization, 65% to 75%, have been reported by (11, 17) highlighting the key role of phototherapy in the management of ABO-incompatible neonates.

The direct antiglobulin test (DAT) was positive in 35% of neonates and was significantly associated with higher rates of phototherapy, IVIG administration,

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exchange transfusion, anemia, and reticulocytosis (Table 3). Neonates with a positive DAT also had significantly higher peak serum bilirubin levels than neonates with a negative DAT (Table 4). These findings support the role of immune-mediated hemolysis in increasing disease severity and treatment requirements. The DAT detects antibodies bound to the surface of the neonatal red blood cell and is therefore an indirect marker of ongoing immune-mediated hemolysis (6, 14). The accelerated destruction of erythrocytes in DAT-positive neonates results in increased bilirubin production and a greater likelihood of developing severe hyper-bilirubinemia (5, 6). These findings support the role of immune-mediated hemolysis in the pathogenesis of ABO incompatibility and underscore the importance of laboratory evaluation in identifying neonates at increased risk of severe disease. Previous studies have also observed that DAT-positive neonates and those with high bilirubin tend to have more severe hemolysis and consequently require more intensive treatment (7, 14, 15). Early identification of high-risk patients may therefore enable timely intervention and reduce the risk of complications (16).

The frequency of IVIG administration and exchange transfusion observed in the present study is similar to findings reported in recent literature. Previous studies have reported phototherapy requirements of between 65% and 75%, IVIG administration of between 15% and 25%, and exchange transfusion rates of less than 10% (11, 12, 13). The results of the present study are therefore consistent with international and regional data, indicating that treatment patterns among neonates with ABO incompatibility remain relatively similar across different healthcare settings (18, 19).

Mechanistically, IVIG is believed to reduce hemolysis by blocking Fc receptors on macrophages and thereby decreasing antibody-mediated destruction of erythrocytes (12). This reduction in hemolysis decreases bilirubin production and may prevent progression to exchange transfusion. Exchange transfusion remains an effective rescue therapy because it simultaneously removes circulating bilirubin, sensitized erythrocytes, and maternal antibodies from the neonatal circulation (13,19).

Complication rates in the present study were relatively low. The most common complication was anemia, while bilirubin encephalopathy was reported in only a small percentage of neonates. Anemia is an expected consequence of ABO incompatibility because antibody-mediated hemolysis results in destruction of circulating red blood cells (4, 6). Similar findings have been reported by Al-Saedi and Al-Khars, Singh and Kumar, and Emokpae and Adeyemo, who observed that severe neurological complications are uncommon when early diagnosis and treatment protocols are implemented (4, 15, 18). Bilirubin encephalopathy develops when unconjugated bilirubin crosses the immature blood-brain barrier and accumulates within neuronal tissues, particularly the basal ganglia (8). The low rate of bilirubin encephalopathy observed in the present study may therefore be attributed to prompt recognition, close monitoring, and timely therapeutic intervention before bilirubin concentrations reached neurotoxic levels (16, 17). These findings emphasize the importance of maintaining effective screening and

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management strategies within neonatal care units.

Another important observation was the longer duration of hospitalization among neonates requiring IVIG or exchange transfusion. Neonates with severe hyperbilirubinemia often require repeated laboratory monitoring, prolonged phototherapy, and additional supportive care, resulting in increased hospital stay. Similar findings have been reported in studies evaluating outcomes of ABO incompatibility and hemolytic neonatal jaundice, where disease severity was directly associated with prolonged hospitalization and increased healthcare utilization (7, 15, 18). The longer hospital stay observed in the present study likely reflects both the severity of hemolysis and the need for close monitoring following advanced therapeutic interventions. Early detection and prompt management could therefore help reduce the duration of hospital stay and lessen the burden on healthcare facilities (16).

The demographic profile of the present study was also comparable to previous reports. Male neonates constituted a slight majority of cases, although ABO incompatibility affected both genders almost equally (10, 15, 18). The mean gestational age and birth weight of the study population were within the normal range for term neonates, indicating that significant hyperbilirubinemia due to ABO incompatibility can occur even in otherwise healthy neonates (3, 4, 9). Since ABO incompatibility is determined primarily by maternal-fetal blood group differences rather than neonatal maturity or birth weight, severe jaundice may develop even in neonates without other recognized risk factors (6). These observations further support the need for careful monitoring of all neonates with suspected blood group incompatibility irrespective of baseline clinical status.

The findings of this study provide useful local data regarding the clinical profile, treatment requirements, and outcomes of term neonates with ABO incompatibility admitted to a tertiary care hospital. Given the limited local literature available on this topic, the study contributes valuable information that may assist clinicians in identifying high-risk neonates and optimizing treatment strategies (10, 16)

Although the study provides important clinical insights, it was conducted at a single center and included only term neonates admitted to one tertiary care facility. Therefore, the findings may not be fully generalizable to all neonatal populations. Nevertheless, the study offers a useful overview of current treatment practices and outcomes in neonates with ABO incompatibility and supports the continued importance of early diagnosis and evidence-based management (6, 18, 19).

Conclusion

ABO incompatibility should continue to be recognized as a clinically significant cause of neonatal jaundice in term infants requiring careful assessment and timely management. Standardized protocols, structured monitoring, and evidence-based treatment approaches remain essential to reduce morbidity and prevent avoidable complications.

Early recognition of ABO incompatibility and close monitoring of bilirubin levels are essential for timely identification of neonates at risk of developing severe disease. Prompt initiation of phototherapy, appropriate use of IVIG, and timely exchange transfusion when

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indicated play a vital role in preventing complications and improving clinical outcomes. The low frequency of severe complications observed in this study highlights the benefits of structured management and adherence to established treatment protocols.

Future Recommendations

Further multicenter studies with larger sample sizes are recommended to validate these findings and improve their generalizability across different healthcare settings and populations.

Study Limitations

This study was conducted at a single tertiary care center and included only term neonates with ABO incompatibility. Therefore, the findings may not be generalizable to all neonatal populations. In addition, long-term neurodevelopmental follow-up was not performed. Future multicenter studies with larger sample sizes and long-term follow-up are recommended.

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Conflict of Interest

The authors declare that there is no conflict of interest regarding this study.

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