The Pattern of ABO Incompatibility in Neonates in Tikur Anbessa Specialized Hospital (TASH), Addis Ababa

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Abstract

Back ground: *ABO incompatibility disease is a major morbidity and health problem of neonates that did not get due attention. To our knowledge, literature informing about ABO incompatibility disease in the country is scanty, despite considerable numbers of neonates admitted to newborn units of the few health institutions found in the nation.*

Objective: *To describe the pattern of ABO incompatibility and modes of therapy and assess outcome of management of these neonates in Pediatrics and Child Health Department, Faculty of Medicine, Addis Ababa University, Newborn Unit.*

Methods*: A retrospective study of 155 newborns with ABO incompatibility admitted to Tikur Anbessa Specialized Hospital Newborn Unit from January 1, 2002 to Dec 31, 2003 was conducted. Data were collected from the charts using prepared questionnaire and then analyzed.*

Results: *Neonates with blood group A and B were found to be 51.6% and 48.4% respectively. The number of neonates with the first birthorder was 82(52.9%) and as the birthorder increases, a decrement in frequency was noted. Newborns who were initially presented with jaundice on admission were 119 (76.8%). Hyperbilirubinemia was seen in 90(85.0%) of neonates and 73 (47%) patients had anemia of varying severity. ABO incompatibility and hemolytic disease of the newborn was found in 105 (67.7%) and 16 (10.3%) of the neonates respectively. Phototherapy was rendered to 80 (51.9%) and double volume blood exchange transfusion was done on 34(22.1%) of the patients. With these measures, majority of them 147(94.8%) got improvement and discharged. Two patients developed kernicterus and six neonates died.*

Conclusion: *Neonates with blood group A and B who were born to blood group O mothers developed ABO incompatibility and hemolytic disease of the newborn. These newborns can be managed at large with phototherapy and in some with double volume exchange transfusion.*

Introduction

ABO incompatibility disease is a major morbidity and health problem of neonates that did not get due attention. It is limited to mothers of blood group 'O' and affects neonates of blood group 'A' or 'B'. Though this relationship of incompatibility occurs in 15 percent of pregnancies, evidence of ABO incompatibility disease is found in only 3 percent of pregnancies and it necessitates exchange transfusion in only 1 in 1000 to 1 in 4000 pregnancies (1).

First born infants have a 40-50 % risk of symptomatic disease. Hemolysis associated with ABO incompatibility has similar physiological mechanism to that of Rh hemolytic disease in that maternal antibody enter the fetal circulation and react with 'A' or 'B' antigen on the erythrocyte surface(2, 3). The presence of IgG anti-A or anti-B antibody in type 'O' mothers explains why hemolysis due to ABO incompatibility frequently occurs during the first pregnancy without prior sensitization (3). Progressive severity of the hemolytic process in subsequent pregnancies is a rare phenomenon; if at all it happens, it tends to become milder (3).

In ABO incompatibility disease, red blood cell destruction would appear to result primarily from extravascular hemolysis, since hyperbilirubinemia predominates and there is little if any evidence of intravascular hemolysis. A prominent feature of ABO hemolytic disease is the presence of microspherocytosis (1).

Symptomatic clinical disease is compensated mild hemolytic anemia with reticulocytosis, microsphrocytosis and early onset of unconjugated hyperbilirubinemia (3). Jaundice is the sole physical manifestation of ABO incompatibility with a clinical significant level of hemolysis. The onset is usually with in the first 24 hours of life (3). In most cases infants become minimally pale and jaundiced, and hepato-splenomegaly is uncommon (3). Neonatal Jaundice caused by other causes will worsen in the presence of ABO incompatibility, and kernicterus has been reported in this set up (2).

The diagnosis of ABO hemolytic disease is often difficult because there are no specific diagnostic tests, and the disorder probably represents only one end of a spectrum of disease that afflicts most ABO incompatible infants (1). Usually the diagnosis is suspected when hyperbilirubinemia appears in the group 'A' or 'B' neonate of 'O' blood group mothers, and it may first require the exclusion of other causes of hyper-bilirubinemia. Jaundice appearing in the first 24 hrs is particularly characteristic of ABO hemolytic disease (4), and its anemia may be mild to moderate or may not exist (1). Evidence of iso-immunization is difficult to interpret, because the coombs' test may be negative or only weakly positive. A positive coombs' test in ABO incompatibility infant doesn't necessarily indicate a disease. It has been observed that one third of all 'A' or 'B' babies of 'O' mothers have a positive direct coombs' test. The coombs' test is not specific for ABO hemolytic disease, because these tests are also frequently positive in infants who are not affected with the disease (4). Due to presence of very little antibody on red blood cells, the direct coombs' test is often weakly positive at birth and may become negative by 2nd or 3rd day of age (2).

The diagnosis of ABO hemolytic disease is supported by findings like indirect hyperbilirubinemia, jaundice during the first 24 hours, an 'A' or 'B' baby of 'O' mothers, increased number of microspherocytosis in the blood, and increased erythrocyte production which is evidenced by reticulocytosis (4).

Treatment of the disease is directed primarily toward the prevention of hyperbilirubinemia. Phototherapy reduces the need for exchange transfusion. Mild cases of ABO incompatibility generally may require phototherapy where as exchange transfusion is indicated for those with more severe hemolysis (5). Thus, current guidelines for treatment of hemolytic disease of the newborn make no differentiation between ABO and Rh incompatibility (6).

For infants with ABO incompatibility, the overall prognosis is excellent. Timely recognition and appropriate management of rare cases with aggressive ABO hemolytic disease may prevent any potential morbidity (3).

The information regarding pattern of ABO incompatibility disease among Ethiopian neonates is scanty even though considerable number of neonates have been admitted to the newborn unit of Tikur Anbessa Specialized Hospital. To our

knowledge, no literature informing about ABO incompatibility disease among neonate is found in the country, and this study may attempt to show clinical presentation, management and outcome in a referral teaching hospital.

Materials and methods

Study design: This was a retrospective descriptive study of ABO incompatibility cases admitted to Department of pediatrics and Child Health, Newborn Unit from Jan. 1, 2002 to Dec 31, 2003.

Study population: The study population included in the study were all cases of ABO incompatibility newborns admitted to the hospital during the stated time.

Inclusion and exclusion criteria: Term newborns with gestational age greater than 37 weeks and birth weight of greater than 2500 gm were included in the study, if admitted and found to have ABO incompatibility. Hyperbilirubinemia due to other causes and charts with incomplete investigation were excluded from the study. Anemia (Hct<30%), presence of polychromasia, significant neonatal hyperbilirubinemia greater than 20 mg/dl and reticulosite count greater than 5% were considered in the evaluation of ABO Hemolytic Disease of the Newborn (HDN).

Data collection: the charts of all ABO incompatibility cases admitted to Department of Pediatrics and Child Health, TASH from Jan 1, 2002, to Dec31, 2003 were retrieved from ward's discharge logbook and patients' medical records, after obtaining permission from the department. Individual data like socio demographic characteristics, including age at admission in hours, their sex, blood group, their birth order, clinical history and findings including age at which time jaundice first detected in hours, presence of pallor, jaundice, hepatomegally and splenomegally was retrieved and transcribed into a purposeful structured format. Laboratory results such as Bilrubin direct and total, hematocrite, reticulosite count, blood morphology, direct coombs' test during and after they were admitted was also recorded. Type of ABO incompatibility, mode of therapy and its out come was also recorded by the principal investigator.

Analysis: Data that was transcribed in the purposeful structured format was further entered and cleaned using EPI info version 6 statistical software and was analyzed using SPSS version 10 statistical package, by the principal investigator. Continuous variables were categorized into meaningful nominal variables, and frequency, proportions and rates of major variables were calculated as applicability.

Operational definitions:

ABO incompatibility: incompatibility state with no disease manifestation.

ABO incompatibility disease: predominance of hyperbilirubinemia with no sign of hemolysis.

ABO hemolytic disease: hyperbilirubinemia with significant hemolysis and microsperocytosis in the peripheral smear.

Neonatal hyperbilirubinemia: total serum bilirubin level greater than 12mg/dl in the term baby

RESULTS

In this study, 155 newborn with either 'A' or 'B' blood group that were born to 'O' mothers were included. Eighty (51.6%) of them were found to have blood group 'A' and the remaining were newborns with the blood group 'B'. Slight male preponderance with male to

female ratio of 1.3:1 was found. The number of neonates with the first birthorder was 82 (52.9%). As birth order increases, a decrement in frequency was noted (Table1).

Majority of the newborns, 119 (76.8%) were initially presented to the hospital neonatology unit with clinical finding of jaundice. Few of them had pallor, hepatomegaly and splenomegaly.

The remaining 25 (%) neonates were found to have no clinical finding signifying of ABO incompatibility disease during admission. (Table2).

After admission to the newborn unit, 120 neonates were subjected to various investigations.

Neonatal hyperbilirubinemia due to ABO incompatibility was seen in 90 (85%) of neonates out of whom 28 (23.3%) newborns were found to have total serum bilirubin level > 20mg/dl. Almost half of the newborns 73 (47%) developed anemia of varying severity. Reticulocyte count above 5% was seen in 16 (13.3%) of the patients. Evaluation of blood morphology revealed normochromic normocytic cells (NCNC) and polychromasia in 112(93.3%) and 8 (6.7%) of the newborns respectively. No microspherocytosis was reported. Direct coombs' test was positive only in one neonate (Table 3).
The pattern of ABO incompatibility was also assessed and ABO incompatibility disease was found in the majority 105 (67.7%) of these newborns. Few of the patients, 16 (10.3%) developed ABO hemolytic disease. ABO incompatibility with out significant illness was detected in the remaining newborns, 40 (25.8%). Among these 40 neonates, 11 were admitted for polycythemia and the remaining for different medical problems other than hyperbilirubinemia (Table 4). The modes of therapy given to these patients were also evaluated. Most of them, 80 (51.9%) were put under phototherapy. Double volume exchange blood transfusion was done for 34 (22.1%) of the neonates (Table 5). Majority of them improved and discharged with the above management. Two of the patients developed features of kernicterus. Six of the admitted neonates died (Table 5).

DISCUSSION

In this survey, the number of neonates with ABO incompatibility among the first birthorder was 52.9%. This is comparable with previous finding and confirms the fact which states unlike Rh disease, it occurs with equal frequency in the newborns of primipara and multipara (3). First pregnancies are likely to be affected because maternal sensitization occurs in life through contact with 'A' and 'B' antigen. The disease doesnt worsen with subsequent affected pregnancies; if at all it happens it tends to become milder (7).

Icterus is often the sole physical manifestation of ABO incompatibility with a clinical significant level of hemolysis (2). In this review, this was confirmed by the fact that majority of these newborns 119 (76.8%) with ABO incompatibility were presented with manifestation of jaundice. Total bilirubin level greater or equal to 20 mg/dl after the time of admission was seen in 28 (23.3%) of the neonate. This finding nearly goes with a conclusion which signifies that in 10-20% of the affected neonates, the unconjugated serum bilirubin level may reach 20 mg/dl or more unless phototherapy is administrated earlier (8).

In this study, anemia with Hct less than 30% was seen in 15 (9.6%) neonates. This finding is unexpectedly high and may be attributed to the small sample size. Severe anemia was rare and the only risk to the newborns with ABO incompatibility was severe hyperbilirubinemia (6).

Characteristic features of hemolytic disease due to ABO incompatibility in this study showed Reticulosite count greater than 5 % in 16 (13.3%) of the neonates. This shows that there was significant number of neonates with on going hemolysis. Polychromasia was found in 8 neonates where as microsphrocytosis which is the hallmark of the hemolysis in ABO hemolytic disease was not reported at all. This could be due to failure of laboratory technicians to look for microspherocytosis and other feature of RBC hemolysis in ABO hemolytic diseases which may need physician's information for careful observation. Because there is very little antibody on the RBC, the direct antiglobulin (coombs' test) is often weakly positive at birth, and may become negative by 2-3 days of age (2). In this review, among 120 neonates who were tested for direct coombs', only one was found to be positive. This could be attributed to technical failure or most of the neonates were subjected to the test after 48 hrs of their life at which time the test is expected to be negative (2).

ABO hemolytic disease was seen in 16 (10.3%) of the neonates. The absence of microsphrocytosis in this survey was found to be a major drawback to diagnose and confirm it.

The presence of ABO incompatibility disease was observed in 105 (67.7%) of the neonates which was also true in other studies. The only risk of ABO incompatibility to the newborn is mainly hyperbilirubinemia (6).

Current guidelines for treatment of HDN make no difference between ABO and Rh incompatibility (6). Mild cases of ABO incompatability generally require phototherapy, where as exchange transfusion is indicated with more severe hemolysis (3). In this survey most of the patients 80 (51.9%) were treated only with phototherapy. This finding is similar to the previous one which says phototherapy is highly effective in the treatment of ABO HDN (6). Double volume exchange transfusion was done for 34 (22.1%) of the neonates. This observation is nearly comparable with other studies (1-7). Majority of the neonates 145 (93.5 %) improved and discharged after treatment with photo-therapy 51.9 % and double volume exchange transfusion for the other 22.1%. This shows that proper management after detection of the risk group saves the lives of the victims with ABO incompatability disease.

The last but not least finding was the immediate complication of the illness noted in this survey. Two of the newborns who came late developed presumed kernicterus. Six of the neonates died. One of the deaths was on its arrival, and had hematocrite of 10%. The remaining five neonates died of a presumed sepsis after the procedure of double volume exchange transfusion. These complications and death would have been prevented if the patients detected earlier and proper measures were taken.

Limitations: Some of the charts were lost or displaced and there was difficulty in finding them. In others, the diagnosis of ABO incompatibility was not put in the problem list when the newborn was

admitted primarily for causes other than ABO incompatibility. These had negative effect to make the study more complete.

CONCLUSION

Some of the neonates with blood group A and B who were born to O mothers developed ABO incompatibility and hemolytic disease of the newborn. These newborns can be efficiently managed at large with phototherapy and in some with aggressive disease with double volume exchange transfusion, if they can be recognized and investigated early at a proper time.

RECOMMENDATION

This study recommends screening of the newborn with ABO incompatibility before discharge from nursery. All neonates born to 'O' mothers should be screened for their blood group, and should be observed for jaundice. This early detection and appropriate management of those rare infants with aggressive ABO hemolytic disease helps to avoid any potential morbidity and mortality related with the disease, and mothers with blood group 'O' should be cautious when their baby got jaundice.

Laboratory technicians should be informed to look for microspherocytosis, Polychromasia, fragmented red blood cells and other feature of hemolytic disease on the peripheral smear for accurate diagnose of ABO hemolytic disease of the newborn.

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Table1. Socio-demographic characteristic of Neonates with ABO incompatibility

Characteristics	Number	Percent
Age at admission (N=155)		
	< 12 hrs	65	41.9
	12-24 hrs	10	6.5
	>24 hrs	80	51.6
Sex (N= 155)		
	Male	88	56.8
	Female	67	43.2
Blood Group(N=155)	A	80	51.6
	B	75	48.4
Birthorder (N= 155)	First	82	52.9
	Second	36	23.2
	Third Or More	37	23.9

Table2: Clinical history and findings of neonates with ABO incompatibility

Investigation	*Number*	*Percent*
Age at which jaundice First detected (N=130)		
<12 hrs	3	2.3
12-24 hrs	13	10.0
>24 hrs	114	87.7
Clinical Finding (N= 155)		
No Finding	25	16.1
Pallor	4	2.6
Jaundice	119	76.8
Hepatomegaly	4	2.6
Splenomegaly	3	1.9

Table 3: Laboratory result of neonates with ABO incompatibility

Investigation	Number	Percent
Bilirubin- total (n=120)		
	< 12 mg/dl	30	25.0
	12- 20 mg/dl	62	51.7
	>20 mg/dl	28	23.3
Bilirubin – direct (n= 120)		
	< 2 mg/dl	113	94.2
	2-3 mg/dl	5	4.2
	> 3 mg/dl	2	1.6
Hct (n=155)		
	<20%	2	1.3
	20-30%	14	9.0
	30-45%	57	36.7
	> 45%	82	53.0
Retic Count (n= 120)		
	<5%	104	86.7
	5-10%	12	10.0
	>10%	4	3.3
Blood Morphology (n=120)		
	NCNC	112	93.3
	Polychormasia	8	6.7
	Microspherocytosis	0	0
Direct coombs' test (n =120)		
	Negative	119	99.2
	Positive	1	0.8

Table 4: Pattern of ABO incompatibility in the neonates admitted to newborn unit.

Pattern (n=155)	number	Percent
ABO incompatibility	40	25.8
ABO incompatibility disease	99	63.9
ABO hemolytic disease	16	10.3

Table 5: Mode of treatment and out come of therapy of neonates with ABO incompatibility

Mode of therapy (n=154)	Number	Percent
No treatment	40	26.0
Photo therapy	80	51.9
Both photo therapy& exchange transfusion	34	22.1
Out come of therapy (n=155)		
Improved and discharged	147	94.8
Developed kernicterus	2	1.3
Died	6	3.9

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