A Review of Rhesus Iso-Immunization in a Nigerian Obstetric Population

Adeniran O. Fawole*, Oladapo S. Sotiloye*, Kehinde I. Hunyinbo*, A. Durodola*, S.I. Omisakin*, A.O.Bale*, A. Sadoh**, U.A. Udo, Ayodele O. Oladimeji* and E. Oladipo Otolorin* #.***

Departments of *Obstetrics & Gynaecology, **Paediatrics and ***Pathology, Federal Medical Centre, Abeokuta, Nigeria and #Regional Centre for Quality of Health Care, Makerere University, Kampala, Uganda.

Abstract

Context: *Haemolytic disease of the newborn, a problem that has not been sufficiently investigated in the Nigerian population, leads to significant perinatal morbidity and mortality.*

Objectives: *To determine the incidence of Rhesus (Rh) isoimmunization and the utilisation rate of Rh-immunoprophylaxis in our population.*

Methods: *A review of the clinical records of all Rh-negative pregnancies, booked at the Federal Medical Centre, Abeokuta between July, 1996 and June, 2000. The mothers' and infants' records were analysed for age, parity, ante-natal antibody status and some selected characteristics in the infant.*

Results: *Seventy-seven Rh-negative pregnancies were managed, accounting for 2.6% of the total obstetric population. Those who received immuno-prophylaxis following previous abortions and deliveries were 15.4 % and 38.2% respectively. Initial testing, at booking, for sensitization was not done in 36.5% of the women, while 63.4% had no follow-up testing. The incidence of ante-natal sensitization was 1.3%. The time of onset of neonatal jaundice was 26.5 ± 14.6 hours (mean ± SD) in Rh-positive infants, compared to 44.4 ± 17.8 hours in Rh-negative infants (p = 0.07). The haematocrit of both groups of infants were similar [42.8 ± 5.8 versus 44.5 ± 5.3; p = 0.6]. There was no perinatal death. The partners' Rh-status was determined in 59.7% and the infants' Rhesus group in 71.6%. Immunoprophylaxis rate was poor (44.8%). The majority of those who declined immunoprophylaxis did so for financial reasons.*

Conclusion: *The risk of haemolytic disease of the newborn with its attendant perinatal morbidity and mortality is real in our community, yet the rate of Rh-immunoprophylaxis remains quite low in our obstetric population.*

Key Words: Rhesus Blood Group, Pregnancy, Isoimmunisation. [Trop J Obstet Gynaecol, 2001, 18: 69-72

Introduction

Haemolytic disease of the newborn is becoming relatively uncommon in modern practice. Perinatal mortality from haemolytic disease of the newborn is also on the decline [1,2]. This decline has been mainly due to the effect of the utilisation of Anti-D prophylaxis within the last four decades, thus reducing the number of pregnancies resulting in sensitisation.

The problem of hemolytic disease of the newborn has not received sufficient attention in our population. This may be partly due to the low prevalence of Rhesus (Rh) negative blood group in Negroid races compared with Caucasian. In a recent survey of Rh blood groups in healthy Nigerian infants, Omotade *et al* [3] reported an incidence of 4.8% Rh-negative individuals. This study is designed to evaluate the incidence of Rhesus immunization and the utilisation rate of Rhesus immuno-prophylaxis in the obstetric population of a tertiary health care center in south-western Nigeria.

Materials & Methods

This was a descriptive study. The case notes of all Rh-negative pregnant women managed in this Hospital between January 1996 and June, 2000 were retrieved. All the women were managed according to the established protocol in the unit. At booking, the ABO and Rh (D) blood groups were determined using standard tube technique. The presence of antibodies was determined in Rhesus negative women using standard techniques.

Rhesus negative women were followed up with antibody screening (and titration) at 4-weekly intervals after the 28th week of gestation. Fetal well being was monitored in sensitised women by serial ultrasound and weekly non-stress test. Sensitised women were delivered at 38 weeks, or earlier if the fetus was compromised.

Correspondence: Dr. A.O. Fawole, Reproductive Health Care Centre, Department of Obstetrics & Gynaecology, Federal Medical Centre, P.M.B. 3031 Abeokuta, Nigeria.

At delivery, a cord blood sample was obtained for the infant's ABO and Rh blood group, haematocrit, serum bilirubin and Coomb's test. Where appropriate, anti-D immunoprophylaxis was administered within 72 hours of delivery. The babies were also followed up with serial monitoring of serum bilirubin and physical examination for jaundice.

The women's biodata, parity, previous history of administration of anti-D globulin, the partner's blood group, gestational age at booking and delivery and the antibody status at booking were collected on a data sheet. Information was further recorded from the case notes of babies of Rhesus negative women admitted into the neonatal unit for neonatal jaundice. Data entry was done with dBase IV [4] software. Data analysis was done with SAS [5] software. Comparisons of means were done with the Student's t-test. For the same period, the Blood Bank's register of blood donors was reviewed and the proportion of Rh-negative donors identified.

Results

During the study period, a total of 2,967 women were booked in the unit, of whom 77 were Rhesus (D) negative. The frequency in the study population was thus 2.6%. Within the same period, there were 171 Rhesus negative individual's among 3 483 blood donors at the institution's blood bank. The incidence in the general population was thus 4.9%. Fourteen patients (18.2%) were primigravida, 16 (20.8%) were nulliparae with previous history of abortion and 47 (61.0%) were parous. Of the 44 women who gave a previous history of abortion, only 2 (4.5%) received anti-D gamma globulin following the abortion. Only 13 (27.7%) of the parous women had ever received immunoprophylaxis following previous deliveries. All the women were followed up to term. Nine of the women (16.7%) however delivered outside the unit and were lost to follow-up.

At booking, 47 women (61.0%) were tested for the presence of antibodies. None showed evidence of previous sensitization. Twenty-seven women (35.1%) had follow-up antibody testing while the majority of the women (64.9%) had no test. Further analysis of the women who were tested revealed that the majority 15/27 had only one test, 11 had two tests and only one woman had all three tests. The overall pregnancy outcome is shown in Table 1. The four stillbirths were apparently from other complications of pregnancy viz premature rupture of membranes, anaemia in pregnancy and prolonged pregnancy.

Table 1

Overall Pregnancy Outcome

Pregnancy Outcome	Frequency	Percentage
Live	63	81.8
Stillbirth	4	5.2
Abortion	1	1.3
Unknown *	9	11.7
Total	**77**	**100.0**

*Confinements outside the unit

There was no perinatal mortality among women who had follow-up testing. The only woman who had antenatal sensitization was a 30 year-old group A Rh-negative Gravida 3, Para 1^{+1} woman with a history of neonatal jaundice, managed with exchange blood transfusion twice, in her last delivery. She had antibody titre of 1 in 4 at 35 weeks. She had only one follow-up test. She neither had immune prophylaxis following the abortion nor the delivery. The index baby (group O positive) developed jaundice at 4 hours of life and was managed with phototherapy. All infants who developed neonatal jaundice were managed conservatively. None required exchange blood transfusion.

Table 2

Paternal Rhesus Status and Neonatal Jaundice in Infant

Paternal Rhesus Status	Neonatal Jaundice	
	Yes	No
Unknown	6 (42.9%)	18
Positive	8 (57.1%)	26
Negative	0	11
Total	**14**	**55**

$x^2 = 3.35$; $P = 0.19$

The partner's blood group was known in 46 (59.7%) women. Thirty-four (73.9%) were Rh-positive and 12 (26.1%) were Rh-negative. The paternal Rh status and the occurrence of neonatal jaundice in the babies is shown in Table 2. There was no significant relationship between the paternal rhesus status and occurrence of jaundice in the infant ($x^2 = 3.35$; $p = 0.19$). In appropriate cases, all women who required immunoprophylaxis were so counselled. Only 28 women (41.2%), including one post-abortal patient, needed immunoprophylaxis.

With respect to the partners' Rh status and post-partum immunoprophylaxis, 18 out of 31 women (58.1%) with Rh positive partners, 3 out of 10 women (30.0%) with Rh negative partners and 7 out of 25 women (28.0%) whose partners' Rh groups were unknown had post-partum immuno-prophylaxis respectively. Excluding women with Rhesus negative partners, only 25 (44.6%) of 56 women whose husbands were either Rh-positive or with an unknown Rh status had immunoprophylaxis. The infant's blood group was determined in 48 (71.6%) cases. Inclusive of babies with unknown blood groups, only 29 (54.7%) of all mothers who needed immunisation received it.

Table 3

Paternal Rhesus Status and Infant's Rhesus Group

	Infant's Rhesus Group		
	Positive	Negative	Unknown
Paternal Rhesus Status			
Positive	17	6	9
Negative	0	4	4
Unknown	12	5	9

Knowledge of the baby's Rh status appeared to be the strongest indicator for maternal immunoprophylaxis as 24 out of 35 mothers (68.8%) of Rh-positive infants received immunoprophylaxis whereas only one out of 12 (7.7%) and 5 out of 18 (27.8%) mothers whose infants' Rh status were negative and unknown respectively had immunoprophylaxis. Documentation of the infant's serum bilirubin and direct Coomb's test was poor. The paternal Rh status is shown against the infants' Rh status in Table 3. Apparently, only 6 fathers (26.1%) were homozygous recessive (genotype dd), and the majority (73.9%) were either homozygous D or heterozygote Dd. The pregnancy and the infants' parameters were compared in the infant with known blood groups. There was no statistical difference in parity, duration of pregnancy, birth weight, duration of postpartum hospitalization, time of onset of neonatal jaundice and the infant's haematocrit (Table 4).

Discussion

Among our obstetric population, haemolytic disease of the new-born, although rare, appears possible. The sensitization rate in this study is 1.3%. Given the background poor level of immuno-prophylaxis in the population, this sensitisation rate is low, especially when compared with the 1.2% reported in the United States where 99.5% of eligible women receive prophylaxis [1]. It is also far less than the reported 14% antenatal sensitization from an Australian study [6]. The lower rate may be partly due to fewer Rh-incompatible pregnancies in our population.

Table 4

Comparison of the Course and Outcome of Pregnancy Between Rhesus Negative and Rhesus Positive infants

Variable	Rhesus Negative Infant Mean ± SD	Rhesus Positive Infant Mean ± SD	*p*
Parity	1.7 ±0.7	1.6 ± 0.8	0.7 (NS)
Duration of Pregnancy (weeks)	35.4± 9.1	37.8 ± 2.1	0.1 (NS)
Birthweight (kg)	2.9 ± 0.6	2.9 ± 0.5	0.8 (NS)
Post partum Hospitalisation (days)	4.2 ± 4.4	4.3 ±2.5	0.7 (NS)
Onset of Neonatal Jaundice (hours)	44.4 ±17.8	26.5 ± 14.6	0.07(NS)
Infant's PCV(%)	44.5 ± 5.3	42.8 ± 5.8	0.6 (NS)

NS: Not Statistically Significant.

Among the suggested factors affecting maternal sensitization viz frequency of feto-maternal transfusion, individual response to Rh-positive antigen, strength of antigen on fetal erythrocyte and ABO protection [7], poor response to the Rhesus antigenic stimulus in the majority of our women appears most probable. This notion is supported by the observation that no Rh-positive infant with neonatal jaundice required exchange blood transfusion. It is presumed that all these cases of neonatal jaundice were physiological in origin. The apparent disparity between the prevalence of Rh-negative pregnancies and Rhesus negative individuals in the general population supports a relative infrequency of Rhesus incompatible pregnancies in our obstetric population.

Despite the low sensitisation rate, the present study has demonstrated that the chances of occurrence of haemolytic disease of the new-born are real in our population. We may not overlook the fact that the study reports experience in a specialist unit. Even here, many deficiencies have been highlighted in the antenatal follow-up. It is highly probable that closer monitoring will reveal higher sensitisation rates.

Thus higher perinatal morbidity and mortality rates are likely in the general population. Sensitisation following abortion may be a major factor in our population since between 5 and 10 % of women are at risk of maternal immunisation after spontaneous and induced abortions [8].

Having established the possibility of occurrence of haemolytic disease of the new-born in our practice, there is the need for concerted efforts to minimise morbidity and mortality from the condition. Health education of the population is vital. A special target group should be schoolgirls who should be encouraged to know their blood groups and enlightened on the implications of the Rh group on future childbearing. Another important tool is continuing education for midwives, medical laboratory staff and physicians. This will enhance collaborative efforts at ensuring mandatory blood group testing for all antenatal and abortion cases and adequate follow-up of identified Rh-negative women, and immunoprophylaxis where appropriate.

However, a policy of routine immuno-prophylaxis as shown in this study cannot be sustained in resource-poor settings. Routine determination of the infants' blood group offers a cheaper alternative and a stronger influence in convincing mother who require immunoprophylaxis . Achieving cost reduction of anti-D immunoglobulin calls for inter-sectoral collaboration.

In the face of low prevalence rates, centralisation of care for sensitized pregnancies is suggested for optimal management as advocated by Gollin and Copel [9]. Rhesus iso-immunisation is a public health issue in contemporary obstetric practice in our population. Public health education, continued training of health workers, increased utilisation of immuno-prophylaxis when indicated and early referral of sensitised pregnancies are the keys to minimising perinatal morbidity and mortality from haemolytic disease of the new born. More research is needed to further elucidate this problem in our population.

References

1. Berger, G. S. and Keith, L. Utilization of Rh prophylaxis. *Clin Obstet Gynecol,* 1982, 25: 267-75

2. CESDI. *Confidential Enquiry into Stillbirths and Deaths in Infancy.* Department of Health. London. 1995.

3. Omotade OO, Adeyemo AA, Kayode CM *et al.* Gene frequencies of ABO and Rhesus (D) blood group alleles in a healthy infant population in Ibadan, Nigeria. *West Afr J Med.* 1999; 18: 294–297

4. Ashton Tate. *dBase IV User Manual.* USA. 1991

5. SAS Institute Inc. SAS® Introductory Guide for Personal Computers, Version 6 . Cary, N.C. 1988.

6. Portman C, Ludlow J, Joyce A, Chan FY. Antecedents to and outcomes of Rh (D) iso-immunisation: Mater Mothers Hospital, Brisbane, 1988–1999. *Aust NZ J Obstet Gynaecol,* 1995; 37: 12–16.

7. Keith LG, Berger GS. Prevention of Rh-sensitization after abortion. In: Zatuchni J, Sciarra JJ, Speidel GI (eds). *Pregnancy Termination Procedure, Safety and New Developments.* Hagerstown, Maryland. Harper and Row, PARFR Series on Fertility Regulation. 1979; 294–302.

8. Keith LG, Method MW, Berger GS. Prevention of Rh-immunization after spontaneous and induced abortion. In: Hafez ES (ed). *Advances in Reproductive Health Care.* Lancaster, England. MTP Press. 1984; 353–361.

9. Gollin YG, Copel JA. Management of the Rh–sensitised mother. *Clin Perinatol.* 1995; 22: 545–549.