Rhesus incompatibility amongst child-bearing women in Ile-Ife, South Western Nigeria

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Abstract

Background: *Rhesus (Rh) isoimmunisation is a recognized cause of perinatal mortality and is also a risk factor for neonatal jaundice. It occurs exclusively in parous RhD negative women with at least one prior pregnancy or in women with previous transfusion of incompatible Rh blood irrespective of their parity. Record on the prevalence of Rh negative pregnant women and the incidence and significance of isoimmunisation on pregnancies is sparse in our setting. This study attempts to provide an insight report on pregnancy outcome in Rh negative Nigerian women.*

Materials and Methods: *The blood bank record of all pregnant women from January 2003 to December 2007 was reviewed for their ABO and Rh blood group. All those that were Rh negative and had their deliveries at the Obafemi Awolowo University Teaching hospitals Complex, Ile-Ife had their clinical case notes reviewed for the outcome of their pregnancies.*

Results: *A total of 2159 pregnant women had their blood group screened, 168 (7.8%) were Rh negative. Of those with complete clinical data, 72% had blood group O while none had blood group AB. Only 44.4% and 66.7% of the husbands and babies' blood group respectively were documented; 8.3% of the babies were ABO compatible with their mothers. Only 16.7% of the babies appeared to have Rh incompatibility with clinical jaundice although all had negative serial indirect Coomb' test which was done in 55.6% of cases for antibody titre estimation. The mean total and unconjugated bilirubin levels of 64µmol and 54µmol respectively. None had phototherapy or blood transfusion. The mean birth weight and haematocrit were 3.1kg and 45.1% respectively. All deliveries were un-eventful with administration of anti-D immunoglobulin (1500 IU statum dose) documented in 50% of cases given within 72hours of delivery.*

Conclusion: *The prevalence of Rh negativity amongst pregnant women from this study is 7.8%, suggesting that Rh negative blood group is not uncommon in our population. The neonate with incompatible group had mild haemolytic disease indicating good pregnancy outcome. However, adequate counselling is still required in our child-bearing women to prevent morbidity from Rh incompatibility.*

Keywords: Pregnant women, Rhesus incompatibility, Antiglobulin, Nigeria

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Introduction

The Rh blood group system is clinically the most important of the protein antigens, and remains the commonest cause of haemolytic disease of the newborn (HDN). The antigens are exclusively found on the red cells antigen. The antibodies directed to the antigens are primarily Immunoglobulin G (Ig-G), and rarely fixed complements; the antibody response may either b e primary or secondary. The Rh antigens consist of a family of inherited antigens of which Race and Fisher[1] earlier proposed three pairs: Dd, Cc, Ee. It is now known that the Rh blood group comprise of more than 45 individual antigens[2] of which five are routinely identified: D, C, c, E and e. The absence of the D antigen denotes Rh negativity. Earlier studies by Worledge *et al*[3] put the prevalence of RhD negativity amongst the Nigerian population at 5%, far less than the observed 15% in the Caucasians. Isoimmunisation to Rh antigen is an important cause of perinatal morbidity and mortality in a woman's obstetrics history. Factors responsible for the development and severity of alloimmunisation are many and these subsequently affect the pregnancy outcome. These factors[4] include obstetrics situations e.g. abortions, ante-partum haemorrhage, caesarean section, instrumental delivery, toxaemia of pregnancy; the amount of feto-maternal transfusion and the sub-type of Ig-G antibody (Ig-G3 > Ig-G1). Anti D Ig-G is the main antibody of Rh induced HDN, its screening and detection is invaluable in the prediction and treatment of HDN.[5]

The degree of severity of HDN is determined by the amount of maternal Ig-G anti D titre, the avidity of the antibodies for Rh antigen and the fetal response to haemolysis (Table 1).[4] It is known that majority of newborn with mild disease will not require treatment. Immunoprophylaxis still remain very important in the management of RhD negative women, the use of anti D Ig-G given at 28 and 34 weeks of pregnancy respectively remains the mainstay.[6] The primary mechanism of action of anti D is believed to be immunologic blockade of the Fc receptors (FcR) within the reticulo-endothelial system, while several other yet unclear immunomodulatory mechanism have also been proposed.[7]

The fetal transplancental haemorrhage (TPH) theory proposed earlier[8,9] still suffice till present; RhD positive fetal red cells cross the placental into the RhD negative mother during pregnancy, and at the time of delivery leading to the production of anti Rh antibodies. About 25-30% of RhD negative pregnant women are non-responders.[10,11] ABO incompatibility provides partial protection against Rh immunisation.[10,11] In all, the prevalence of Rh alloimmunisation post ABO compatible pregnancies is 8 to 16% while the prevalence is 1.5 to 2% after delivery of ABO incompatible, RhD positive infants.[4] A prevalence of 9.1% was observed by Onwuahafa et al[12] in Nigerian RhD negative women post delivery in the northern part of Nigeria. As earlier observed, RhD isoimmunisation is not a major cause of neonatal jaundice (NNJ) in Nigeria in variance to what obtain in Caucasian community where RhD isoimmunisation rate is about 18% and accounted significantly to the aetiology of NNJ.[13] The paucity of data on Rh isoimmunisation and the need to determine its significance and associated clinical features in Nigerian pregnant women informed this 5-year retrospective study at the Obafemi Awolowo University Teaching Hospitals Complex, Ile-ife, Nigeria.

Patients and Methods

The ABO and Rh blood group was determined for all patients presenting for antenatal care at booking. Blood groups are routinely determined using tiles method and reverse grouping (using tube method) at room temperature and at 37^0C for ABO and Rh groups respectively. Those that are Rh negative had, additionally, serial indirect Coomb's test for their antibody titre levels at subsequent visits. The frequency of antibody titre estimation is dependent on patient's previous

obstetrics history and the findings during the index pregnancy. The information reviewed on the Rh negative pregnant women in this study was obtained from the blood bank record books and the clinical-notes of the patients that were Rh negative from January 2003 to December 2007. All these patients had their deliveries at the Obafemi Awolowo University Teaching hospitals Complex, Ile-Ife.

Results

A total of 2159 pregnant women had their ABO and Rh blood group determined at the blood bank unit during the study period. Of these, 168 (7.8%) were Rh negative. However, case-notes of 72 (42.9%) of these patients were obtainable for review. The age of patients at booking was 30.6years, while the mean gestational age was 21.1 weeks. Forty eight (66.7%) patients were haemoglobin (Hb) AA, 16 (22.2%) were HbAS while the remaining 11.1% did not have Hb type recorded. 20 (27.8%) were nulliparae and do not have previous history of abortion. The remaining 52 patients were multiparae; 20 (38.5%) of which had previous abortions or stillbirths probably related to Rh incompatibility, eight (11.1%) abortions were unrelated to Rh incompartibility (secondary to pregnancy induced hypertension, eclampsia, diabetes mellitus). Fifty two (72.2%) were of blood group O, 4 (5.6%) and 16 (22.2%) were of blood groups A and B respectively. None of the patients had blood group AB (Table 1). Thirty two (44.4%) of the husbands of these women had their blood group stated {O,8 (25%); A,4 (12.5%); B,12 (37.5%) and AB,8 (25%)}, and of these four were Rh negative. Delivery was uneventful in all the cases, caesarean deliveries (n=16 (22%) were due cephalo-pelvic disproportion and premature rupture of membrane.

The Apgar score was optimal in all the babies at five minutes, however, 12 (16.7%) babies had clinical jaundice with mild elevation of their bilirubin levels. The mean total and conjugated bilirubin levels of 64µmol and 10µmol was obtained in 10 (83.3%) of the 12 neonates with clinical jaundice. None of the babies had phototherapy or exchange blood transfusion. 64 (88.9%) had their birth weight documented with a mean of 3.1kg, while 50% had their haematocrit at birth documented with a mean value of 45.1%. The blood group of the babies were documented in 48 (66.7%) cases (O, 16 {33.3%}; A, 12 {25%}; B, 20 {41.7%}, AB, nil), and of these 8 (16.7%) were Rh negative. Only four (8.3%) of the babies shared the same ABO

Table 1: Table showing the categorization of the degree of severity of haemolytic disease of the newborn (HDN) and percentage incidence

Degree of severity	Description	Incidence (%)
Mild	Indirect bilirubin ≤16-20g/dl, No anaemia, No treatment needed.	45-50
Moderate	Fetal hydrops does not develop, Moderate anaemia, severe jaundice with risk of kernicterus unless treated after birth.	25-30
Severe	Fetal hydrops in utero. Before 34 weeks. After 34 weeks.	20-25 10-12 10-12

blood group with their mothers, the rest had discordant ABO blood group. Hospital stay more than two days was due to maternal factors in 8 (16.7%) of cases and a baby (2.1%) due to hyperbilirubinaemia which was conservatively managed.

Anti-D (1500 iu statum dose) was given in 50% of patients in the index pregnancy, within 72 hours of delivery. Only 13% of the multiparous had received anti-D in the previous pregnancies. Serial indirect Coomb's test was documented only in 55.6% of cases during index pregnancy, and all were negative.

Discussion

The prevalence of Rh negativity amongst pregnant women from this study is 7.8%. This finding suggest that prevalence of Rh negative blood group may be higher than earlier observed,[3] more importantly amongst the people of the South Western Nigeria where the present study was carried out. Earlier, Onwuhafa, *et al*[12] reported the highest incidence of Rh negative pregnancy among the Yoruba ethnic group of the South Western Nigeria in a study carried out in the Northern part of predominantly Hausa ethnic group. There was presence of neonatal jaundice (NNJ) and raised bilirubin levels in 16.7% of the neonates (irrespective of the ABO blood group), although all had mild haemolytic disease of the newborn (HDN) (Table 1), it may not be sufficiently ascribed to isoimmunisation in view of negative antiglobulin tests. However, no other cause of NNJ was documented. Thus, Rh incompatibility in our child-bearing women may not be a significant cause of morbidity or an important cause of NNJ as earlier reported.[13] It is important to note that all the neonates had mild jaundice, and none of them had phototherapy or exchange blood transfusion. The mean bilirubin levels observed in them was 64µmol (0.8mg/dl) and 54µmol (0.6mg/dl) (total and unconjugated respectively), and none had history of blood transfusion.

Previous work have shown that RhD Ig-G1 antibody usually present with a less severe disease;[4] could it be that the less severe RhD Ig-G1 subtype is the antibody transmitted in the Nigerian population? It is however important to note that this does not preclude the use of appropriate prophylaxis of anti RhD, which still remain the gold standard in the management of RhD negative pregnant woman. This is particularly important in the mothers of neonates with evidence of jaundice.

The work done by Lee *et al*[6] affirm the usefulness of anti-D immunoglobulin given during antenatal care. Also, Baptista-Gonzalez et al observed that the use of anti-D immunoglobulin reduced the likelihood of Rh isoimmunisation and concluded that it prevents the additional obstetrics problems in the mothers[14]. However, we believe there is a need to determine if all our cohort of patients will necessarily require anti-D immunoglobulin as suggested by our findings; half of the patients studied had post-partum anti-D immunoglobulin while only 13% of the multiparae had anti-D immunoglobulin in their previous pregnancies and 23% showed clinical evidence of Rh incompatibility in the index pregnancy. This becomes imperative in view of the high cost of anti-D immunoglobulin and the poor status of most of our patients. We also opined that efforts should be made to increase awareness amongst patients with Rh negativity, ensure determination and recording of the husband's and baby's blood group in the antenatal clinical notes. These will enhance proper follow-up and clinical management in subsequent pregnancies.

Conclusion

The prevalence of Rh negativity amongst pregnant women from this study is 7.8%, suggesting that Rh negative blood group is not uncommon in our population. Neonates with incompatible Rh group had mild haemolytic disease of the newborn indicating less disease

severity and a good obstetrics outcome. However, adequate counselling is still required in our child-bearing women to prevent morbidity from Rh incompatibility.

Limitations of this study

The retrospective method employed exclude un-booked deliveries in whom blood groups were not documented in our blood bank record. Also, not all registered Rh negative pregnant women case files were obtainable for review.

References

1. Race RR. The Rh genotype and Fisher's theory. Blood 1948; 3: 27-42.
2. Walker RH. (ed) Technical Manual, 10th ed. American Association of Blood Banks. Arlington, VA, 1990; 20.
3. Worlledge S, Luzzato L, Ogiemudia SE, Luzzato P, Edington GM. Rhesus immunisation in Nigeria. Vox Sang. 1968; 14: 202-210.
4. Wintrobe Haematology
5. Kai- Liang L, Ning Li, Bi-Juan Li, Jin Yan P, Yiang-Wu Shu, Yun-Ying Yu. Clinical significance of anti D Ig-G screening and titre detection in 286 RhD negative pregnant women. Zhongguo Dang Dai Er Ke Za Zhi 2009; 11(3): 185-187.
6. Lee D, Rawlinson VI. Multicenter trial of antepartum low-dose anti-D immunoglobulin. Transfusion Med. 1995; (1):15-19.
7. Ware RE, Zimmerman SA. Anti-D: mechanisms of action. Semin Haematol. 1998; 35(1): 14-22.
8. Weiner AS. Diagnosis and treatment of anaemia of the newborn caused by occult placental haemorrhage. Am J Obstet Gynaecol. 1948; 56: 717-722.
9. Chown B. Anaemia from bleeding of the fetus into the mother's circulation. Lancet 1954; 1: 1213-1215.
10. Nevanlinna HR. Factors affecting maternal Rh immunization. Ann Med Exp Fenn. 1953; 31(2): 1-4.
11. Bowman JN. Fetomaternal ABO incompatibility and erystoblastosis fetalis. Vox San. 1986; 50: 104-106.
12. Onwuahafa PI, Adze J. Pregnancy in Rhesus negative women in Kaduna, Northern Nigeria. Trop J Obst Gynaecol. 2004; 21: 21-23.
13. Ahmed H. Neonatal jaundice in Nigeria: An overview of four decades of medical research. Nig J Med. 1997; 6(4): 97-104.
14. Baptita-Gonzalez HA, Rosenfeld-Mann F, Leiss-Marquez T. Prevention of isoimmunisation with anti-D gamma globulin. Salud Publica de Mexico 2001; 43(1): 52-58.