Original Research Article

Maternal and perinatal outcome in rhesus antigen negative pregnancy

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Abstract

Background: Nearly 5% of Indian population is Rh negative. When an Rh negative mother gets exposed to Rh positive blood cells, there might be development of Rh antibodies which is known as Rh isoimmunization.
Aim: To find out the incidence and fetomaternal outcome of Rh negative women during pregnancy.
Materials and methods: This was a prospective observational study carried out in Government Victoria Hospital, under the Department of Obstetrics and Gynecology, Andhra Medical College, Visakhapatnam from January, 2019 to December, 2019. All Rh negative pregnant women with incompatible mating were taken into this study. After delivery, Cord blood was collected and sent for baby blood grouping and Rh typing, Hemoglobin concentration, Hematocrit, Serum total and indirect bilirubin values and Direct Coombs test. Neonatal outcome was assessed for weight and APGAR score. The neonate was followed for 72 hours after delivery.
Results: Out of the total 243 neonates, 172 were Rh positive and 71 were Rh negative. Out of 107 multigravidas, ICT was positive in only 2 cases and their antibody titres were less than 1:32 with normal fetal MCA doppler. 143 out of 172 Rh positive neonates developed neonatal jaundice, and 14 out of them required phototherapy.
Conclusion: There is a revolution in the treatment of Rh negative pregnancy after the advent of Anti D. As shown in the present study, there is very less risk of perinatal mortality among Rh positive fetuses due to proper utilization of Anti D.

Key words

Immunoprophylaxis, Neonatal jaundice, Isoimmunisation, Fetomaternal hemorrhage.

Introduction

The Rh factor is the largest and clinically most important protein based blood group system [1]. Levine and Stenson discovered an atypical immune agglutinin in a woman who underwent a still birth in 1939. Later, in 1941, Landsteiner and Weiner discovered Rh antigen. It was first observed in blood of rhesus monkeys and named as Rhesus (Rh) factor. Most of the humans also have a factor which is in common with the rhesus monkey. Those people were classified under Rh positive individuals while those who do not have it were classified under Rh negative individuals [2].

Nearly 5% of Indian population is Rh negative. When an Rh negative mother gets exposed to Rh positive blood cells, there might be development of Rh antibodies. This condition is known as Rh isoimmunization [3].

In a normal pregnancy, fetal red blood cells cross placenta in 5% of cases during first trimester and 46% of cases by the end of third trimester. But, in majority of the cases, Rh isoimmunization occurs as a consequence of maternal bleeding during delivery. About 10 to 15% of Rh negative mothers with Rh positive fetus get sensitized at delivery. This is due to insufficient amount of fetal blood cells to produce primary immunological response [1].

The probability of primary immune sensitization depends on size of inoculum and coexistence of ABO incompatibility between mother and fetus. The greater the fetomaternal hemorrhage, the more the possibility of isoimmunization. If the mother's group is O while father's is A, B, or AB, the frequency of sensitization decreases by 50 to 75%. This is because of destruction of fetal RBCs with A or B antigen by preformed Anti-A or Anti-B antibodies in maternal serum even before sensitization [1].

The incidence of immune response during pregnancy is 1% while during delivery is 10-15%. The initial maternal response to Rh fetal antigen is production of IgM antibodies which are too large to cross the placenta. Later, there will be production of IgA antibodies which cross the placenta and cause fetal blood cell destruction. The time taken for fetomaternal hemorrhage and appearance of antibodies is usually several weeks. Hence, the usage of Anti-D prophylaxis shortly after delivery or sensitizing events inhibits immune response.

Materials and methods

The present study was carried out in 243 antenatal women who attended OPD as well as emergency services in obstetric unit of Government Victoria Hospital, under the Department of Obstetrics and Gynecology, Andhra Medical College, Visakhapatnam. They were investigated from January, 2019 to December, 2019. It was a prospective observational study. All pregnant women with Rh negative blood group with incompatible mating were taken into this study. Detailed history of patients was taken regarding age, address, occupation, gravidity, parity, abortions, D&Cs and any other complications. Status of anti-D prophylaxis was also taken in multigravidas. Any history of jaundice, hydrops fetalis and blood transfusions in previous births was taken. Detailed history about present pregnancy like history of bleeding per vaginum, threatened abortion was taken.

Inclusion criteria

- Singleton pregnancy
- Live fetus in utero
- Husband blood group is positive

Exclusion criteria

- Intrauterine fetal demise
- Multiple gestation
- Failure to give consent
- Husband blood group is negative

Complete general examination was done to the patients. Complete obstetric examination was done for height of uterus, lie and presentation of fetus. Fetal heart sound was noted. Per

vaginal examination was done for those who presented with labour pains. Complete obstetric scan with Biophysical profile with uterine artery, umbilical artery and middle cerebral artery doppler was performed.

Investigations performed were Complete blood counts, Blood grouping and Rh typing, Glucose challenge test with 75 grams of oral glucose, HIV, HBsAg, VDRL, TSH and complete urine examination. Husband blood grouping and Rh typing was done.

Indirect Coombs test was done at 1st visit and was repeated accordingly at 16 weeks, 20 weeks, 24 weeks and 28 weeks for multigravidas. It was done at 20 weeks and 28 weeks for primigravidas. Patients with negative antibody titre were offered antepartum Rh immunoglobulin prophylaxis with 300mcg.

Patients who had spontaneous labour were monitored carefully. Those who do not go to spontaneous labour were induced at 39+6 weeks and monitoring was done. Stripping of membranes and artificial rupture of membranes were avoided. Early cord clamping and active management of third stage of labour was performed. Cord blood was collected and sent for baby blood grouping and Rh typing, Hemoglobin concentration, Hematocrit, Serum total and indirect bilirubin values and Direct Coombs test. Neonatal outcome was assessed for weight and APGAR score. If the neonate Rh status was positive, 300mcg of Anti-D immunoglobulin was given to mother within 24 hours of delivery.

All neonates were thoroughly examined by neonatologist for any congenital anomalies. The neonate was followed for 72 hours for any development of jaundice. The babies with hyperbilirubinemia were sent to special newborn care unit for the advice of neonatologist. Indicated neonates were treated with phototherapy neonatologist. They were advised to attend postnatal clinic after 6 weeks or routine follow up.

Results

Out of the 243 cases, 136 were primigravidas while 107 were multigravidas. ICT was positive in only 2 cases and they are multigravidas. Their antibody titres were less than 1:32 and fetal MCA doppler was normal. Anti-D immune prophylaxis was taken at 28 to 30 weeks gestation by only 51 cases out of 243 cases accounting to 20.9%.

Chart - 1 shows that out of the total 243 neonates, 172 were Rh positive and 71 were Rh negative which accounts to 70.7 and 29.3 % respectively.

Chart - 1: Percentage of Rh negative and positive neonates.

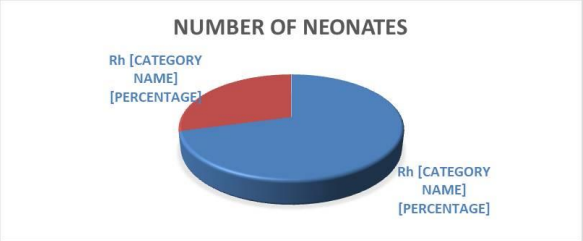


Table - 1 shows that out of the total deliveries, 209 were delivered between 37 to 40 weeks, 12 were delivered before 37 weeks and 22 were delivered after 40 weeks. 218 cases delivered normally, 20 required caesarian section and 5 were delivered by outlet forceps.

Table - 1: Distribution as per gestational age at delivery.

Gestation at delivery	No. of deliveries	Percentage
<37 weeks	12	4.9%
37 to 40 weeks	209	86%
>40 weeks	22	9.05%

Table - 2 shows distribution of various blood groups among the neonates. Out of 243 neonates, 71 were Rh negative, 105 were O positive, 37 were B positive, 21 were A positive and 9 were AB positive.

Table - 2: Distribution of blood groups among neonates.

Blood group	No. of neonates	Percentage
Rh negative	71	29.3%
O+VE	105	43.2%
B+VE	37	15.2%
A+VE	21	8.6%
AB+VE	9	3.7%

Chart - 2 shows that among 107 multigravidas, 58 cases had previous one full term delivery, 18 cases had previous one abortion, 12 cases had previous one full term delivery as well as abortion, 6 cases had previous preterm deliveries, 4 cases had previous two full term deliveries, 4 cases had previous 2 abortions, 3 cases had previous 3 abortions and 2 cases had previous one delivery and two abortions.

Chart - 2: History of previous pregnancies in multigravidas.

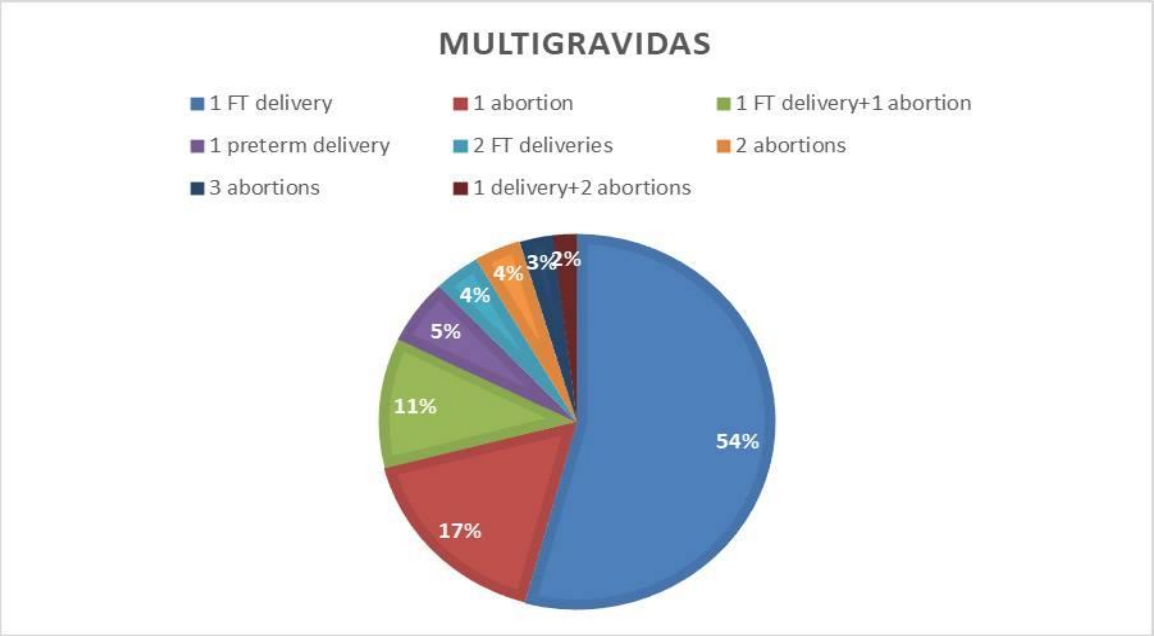


Chart - 3: Status of Anti D prophylaxis in previous pregnancies.

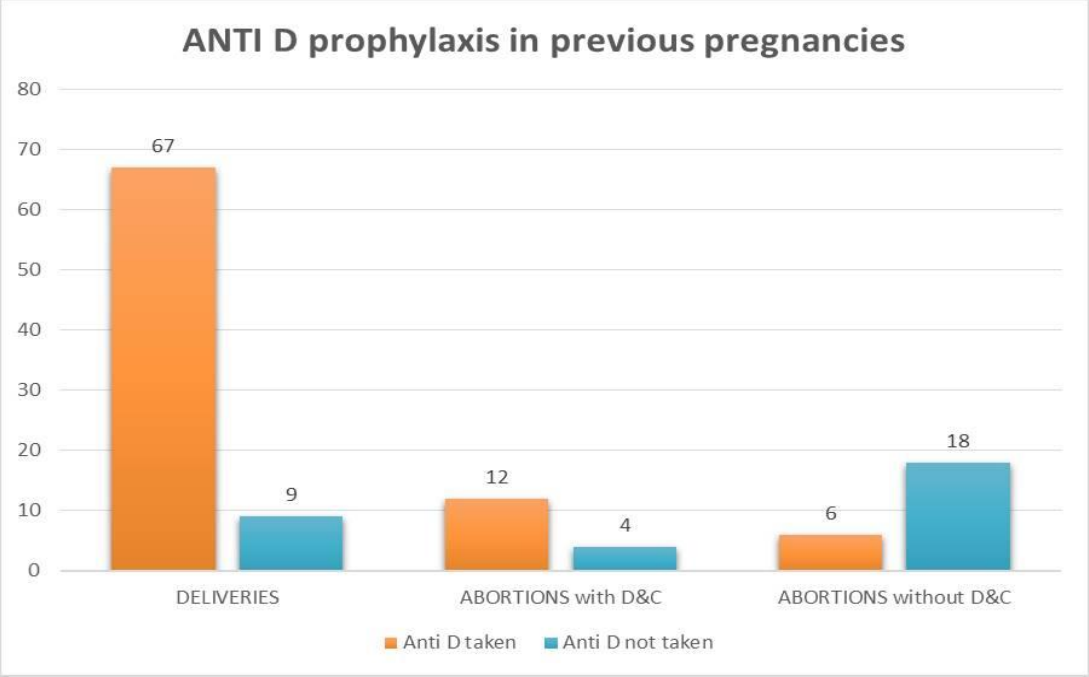


Chart - 4: Distribution of Rh positive neonates as per serum concentration of indirect bilirubin.

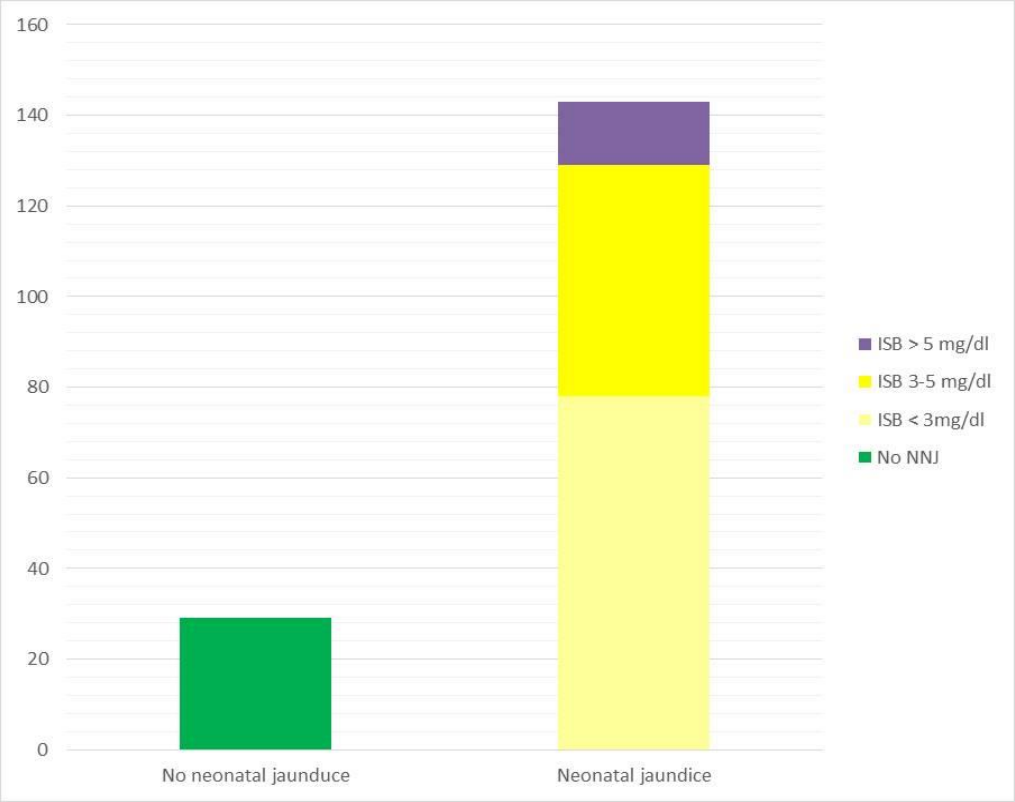
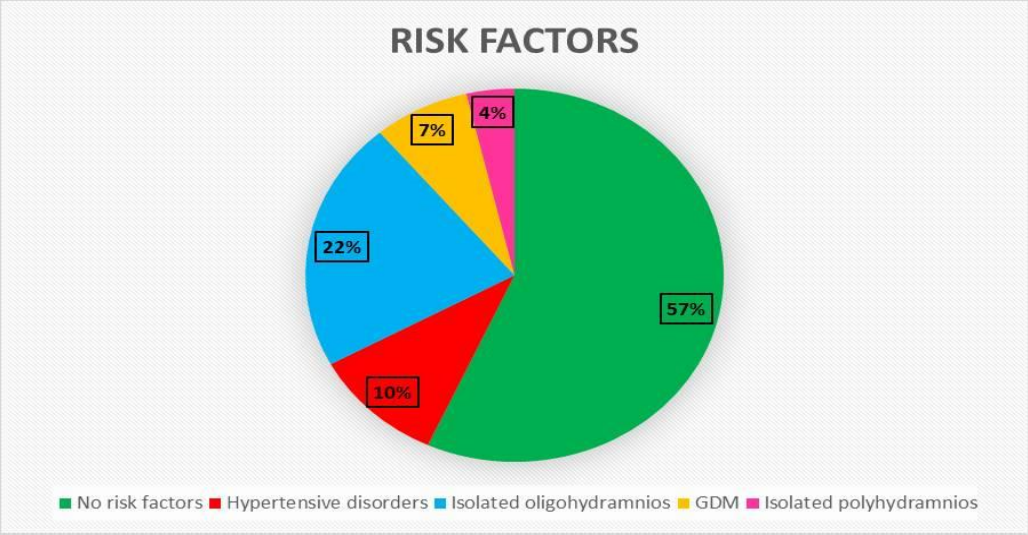


Chart - 5: Obstetric risk factors in Rh negative pregnancy.



Out of 137 previous pregnancies, 92 were full term deliveries, 39 were abortions and 6 were preterm deliveries. Out of 98 deliveries, 76 were Rh positive fetuses and only 67 mothers were given Anti D immunoglobulin post-delivery. Out of 39 abortions, D&C was done in 16 cases, 14 cases were verified by ultrasound and 9 were not verified. Only 12 cases were given Anti D immunoglobulin after abortion.

Chart - 3 shows the status of Anti D immunoprophylaxis in previous pregnancies.

Chart - 4 shows distribution of Rh positive neonates as per serum concentration of indirect bilirubin. Out of 172 Rh positive neonates, 143 neonates developed neonatal jaundice. Out of them, 78 had indirect serum bilirubin level less than 3 mg/dl, 51 had between 3 to 5 mg/dl and

14 had above 5 mg/dl. All the 14 neonates were treated with phototherapy. Among them, 12 were born to multigravidas and 2 were born to primigravidas accounting to 85.7 and 14.3% respectively. This accounted to 16.86% did not develop jaundice, 54.54% had indirect serum bilirubin less than 3 mg/dl, 35.66% had between 3 to 5 mg/dl and 9.79% more than 5 mg/dl.

Table - 3 shows the distribution of hemoglobin concentration among neonates with positive blood group. Among 172 neonates, 170 neonates have no anemia while 2 neonates had mild anemia. None of them required blood transfusion.

Table – 3: Distribution of hemoglobin concentration among neonates with positive blood group.

Hemoglobin concentration	Number of neonates	Percentage
>14gm%	170	98.8%
10-14gm%	2	1.16%
<10gm%	0	0%

Chart - 5 shows the distribution of various obstetric risk factors among antenatal women with Rh negative pregnancy. Out of 243 Rh negative pregnancies, hypertensive disorders were present in 25 cases, isolated oligohydramnios (AFI<8cm) in 53 cases, gestational diabetes in 18 cases and isolated polyhydramnios in 9 cases which accounted to 10.28%, 21.8%, 7.4% and 3.7% respectively.

Discussion

When 1 ml of Rh positive red blood cells enters maternal circulation, 15% women would be immunized. When the quantity increases to 10 ml, this increases to 33% [2]. Nearly, 99% of women have fetomaternal hemorrhage of less than 4 ml at delivery and majority has less than 15 ml.

A single dose of 300mcg Rh immunoglobulin is adequate to cover a fetomaternal hemorrhage up to 15 ml. This should be administered as soon as possible but within 72 hours of delivery. It offers some protection even when given less than 13 days. Recommendations have been made to administer even as late as 28 days [4]. A single dose of 300mcg in the 28th week of pregnancy prevents isoimmunization provided the woman is unimmunized. If she was already immunized, it will not be effective [5].

Prophylaxis after potentially sensitizing events should be administered within 72 hours of event. Potentially sensitizing events in pregnancy include amniocentesis, chorionic villous biopsy, cordocentesis, antepartum hemorrhage, external cephalic version, abdominal trauma (sharp/blunt, open/ closed), intrauterine death, still birth, any therapeutic interventions in utero and delivery (normal/ instrumental/ cesarean section). If pregnancy is less than 12 weeks, it is indicated only following ectopic pregnancy, molar pregnancy or therapeutic termination. The minimum dose is 150 IU or 30 mcg [6].

In India, Federation of Obstetric and Gynecological Societies of India recommend that all patients going for MTP should have documentary proof of blood group of both partners. It recommends routine antenatal prophylaxis of single dose of 300 mcg at 28 weeks followed by post-natal prophylaxis by 300 mcg as soon as possible if the baby in Rh positive and DCT is negative. It also recommends 100 mcg anti-D after the sensitizing event of the first trimester. This post-partum anti-D dose is sufficient enough to neutralize 30 ml of fetal blood and can be given without any quantitative test for fetomaternal hemorrhage. These tests, i.e. Kleihauer Betke test, flow cytometry, and rosette test are not readily available in India, and also cost benefit of such testing has not been determined [7].

Conclusion

With the advent of Anti D immunoglobulin, there is a revolution in the treatment of Rh negative pregnancy. As shown in the present study, there is very less risk of perinatal mortality

among Rh positive fetuses. This is due to proper utilization of Anti D. But there is a high incidence of neonatal jaundice needing NICU admission and phototherapy. The incidence of need for phototherapy was more in neonates born to multigravidas than primigravidas.

All pregnant women should undergo test for blood grouping and typing during first visit. If blood group is negative, husband blood grouping and typing and indirect Coombs test should be performed. They must be counseled regarding importance of Anti-D prophylaxis, Hemolytic disease of the newborn, neonatal jaundice and exchange transfusion. Indirect Coombs test should be repeated necessarily and Rh immunoglobulin should be given at 28 weeks of gestation. The dosage recommended is 300mcg. After delivery, cord blood should be collected and sent for direct Coombs test, indirect bilirubin levels, hemoglobin concentration, hematocrit and most importantly blood grouping and Rh typing. If the neonate is Rh positive, Rh immunoglobulin is again given within 72 hours of delivery. This protocol when followed decreases the chances of isoimmunization.

Rh immunoglobulin is usually being given after delivery. But RAADP (Routine Antenatal Anti-D Prophylaxis) and prophylaxis after abortions need to be encouraged to further decrease the incidence of Rh isoimmunization, especially in rural areas.

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