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FETAL OUTCOME IN Rh NEGATIVE MOTHERS

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ABSTRACT

Background: The objective of this study is to find out the incidence and fetal outcome of Rh negative women during pregnancy. **Methods:** The study consisted of all Rh negative mothers, booked as well as emergency cases coming to Rajkiya Mahila Chikitsalaya, Ajmer, for regular antenatal check up and for confinement from 2018 to 2019. Minimum 100 subjects were taken for study and were followed. Patients with Cardio vascular disease, severe anaemic, Gestational diabetes mellitus and pregnancy induced hypertension were excluded. **Results:** Blood group distribution of newborn: 126 were Rh positive and 34 were Rh negative. Raised Rh antibody titre was not found in any of the 130 cases. Maximum cases was delivered by vaginal delivery. The babies who developed NNHB were managed either by sunrays exposure only or by phototherapy. The babies who had anemia immediately after birth were carefully monitored and considered for exchange transfusion. 10 babies had erythroblastosis fetalis. Out of 160 cases we found 16 intrauterine death. **Conclusions:** In this study it was observed that all those patients though severely affected had good foetal outcome due to safe and proper delivery practise in the institution and prompt management of the newborn. As results all the neonates all the neonates survived except those who had come as IUDs.

INTRODUCTION

With the discovery of the Rh factor by Landsteiner and Weiner 1941, the recognition of its clinical importance and the practical application of this knowledge in therapy constitute one of the great advances of modern research where theory, observation and practice, in the space of a very few years, pieced themselves together to form a coherent picture. Rhesus (Rh) incompatibility refers to the discordant pairing of maternal and fetal Rh type. It is associated with the development of maternal Rh sensitization and hemolytic disease of the neonate (HDN). An individual can be classified as Rh-positive if their erythrocytes express the Rh D antigen; otherwise, an individual is Rh-negative if they do not.

This phenomenon becomes clinically significant if a mother is Rh-negative becomes sensitized to the D antigen and subsequently, produces anti-D antibodies (i.e., alloimmunization) that can bind to and potentially lead to the destruction of Rh-positive erythrocytes. This is of particular concern if a Rh-negative mother is carrying a Rh-positive fetus, which can result in consequences along the spectrum of HDN ranging from self-limited hemolytic anemia to severe hydrops fetalis.1

The incidence of the disease however is now on decline worldwide from 1.3-1.7% in 1980s to 0.17% in 1990s. The proportion of people who are Rh negative also varies according to race. For example, in China and Japan it is most uncommon, and it might be suggested that the elder civilization of the Chinese has, by a process of natural selection, bred out an undesirable gene. In India previously, it was thought that it is present only in Parsis, but afterwards it was detected in others also.2 One of most dreadful implication of ABO incompatibility or Rh incompatible pregnancy is Erythroblastosis foetalis. It is a treacherous hemolytic disease of foetuses and new born which affect less than 1% of all pregnancies, the excessively rapid destruction of erythrocyte which is characteristic of this disease, produces profound anasarca.

Red cell destruction by hemolysis is caused by specific antibodies entering the foetal circulation during pregnancy. These antibodies are produced by mother in response to antigenic stimulation of foetal red cell entering the maternal circulation by the way of placenta. These erythrocytes possess antigenic factor not present normally in the mother and therefore are capable of initiating antibody production.1,2 The incidence of Rh incompatibility in Rh negative women carrying a Rh-positive foetus is about 10% of all Rh-negative pregnancies. Sensitization however occurs only in about 5% of these cases giving an incidence of 6-7/1000 of all the pregnancies and 1-15 Rh negative pregnancies.

First pregnancy is rarely affected, and as a rule the degree of sensitization increase with subsequent pregnancies. Once sensitization has occurred, the clinical and laboratory approach to evaluate and treat the disorder is difficult.3,4 Various studies have been conducted and several are going on to achieve zero incidence of this disease. With the introduction of techniques of Amniocentesis and spectrophotometric analysis of Amniotic fluid, the pregnancy can well be followed up and timely terminated to have best perinatal outcome. The early detection of the disease with raised antibody titre is of utmost importance.

The newer treatment modalities like intra uterine transfusion and Intra venous immunoglobin helps further to reduce the overall mortality and morbidity. When the above techniques are combined with antepartum and postpartum immunoprophylaxis there is a further decline in the incidence foetal complications and perinatal mortality.5,6

METHOD

The study consisted of all Rh negative mothers, booked as well as emergency cases coming to Rajkiya Mahila Chikitsalaya, Ajmer, for regular antenatal check up and for confinement from 2018 to 2019. Minimum 100 subjects were taken for study and were followed.

The clinical history of each patient was recorded in detail :

1. Age, Socio-economic status and parity.
2. The status of Rh antibody titre in the present pregnancy.
3. If multigravida, the history of anti D given in previous pregnancy was recorded.
4. Past fetal outcome (if multipara) was recorded.
5. Any significant past or family history.

Inclusion criteria

- All pregnant women Rh negative.

Exclusion criteria

- Patients with Cardio vascular disease, severe anaemic, Gestational diabetes mellitus and pregnancy induced hypertension were excluded.

Complete general examination of the patients was done which included degree of anemia, pulse, BP, and pedal edema. Systemic examination was done to exclude other medical disorders viz. respiratory disease, CVS disorders, chronic hypertension, chronic nephritis and any other chronic illness. Obstetrical examination complete examination including fundal height, lie and position of the foetus, presentation, AFI assessment was done and FHS was noted. Internal examination was done in patients who presented with labor pains.

Investigation Routine examination of the blood which included blood grouping and typing, Hb%, total and differential blood count, platelets, blood sugar, and urine for the presence of albumin was done by standard method. Husband blood grouping and typing of all the Rh-negative patients was done. Rh antibody titre of the patients was done at first visit and were repeated accordingly at 28 weeks and 32 weeks. Patients whose husbands were Rh positive and having negative antibody titre were offered antepartum Rh 1G immunoprophylaxis. Ultrasonography was done to know the gestational age, foetal wellbeing, amount of liquor, placental grading, maturation and to rule out any congenital malformations. The USG was repeated at regular intervals as per need.

The labor was monitored carefully, and the mode of delivery and the outcome of labor was studied in detail. Inj. methergine was not given after delivery and the placenta was examined for hyperplacentosis. Cord blood was collected and was sent for ABO/Rh typing, Hb% serum bilirubin (total, direct and indirect) and direct Coomb's test to know the neonatal status. Baby was thoroughly examined for any obvious congenital anomaly and weight, sex and condition was noted particularly for hydrops foetalis. If neonate was Rh positive, then the mother was given postpartum immunoprophylaxis within 24 hours of delivery.

The new born were followed for 3 days and were watched for the development of Jaundice. The babies who development NNHB were managed either by sunrays exposure only or by phototherapy. The babies who had anemia immediately after birth carefully monitored and considered for exchange transfusion. They were advised to attend postnatal clinic for check-up after 6 weeks of delivery.

Statistical analysis

Data will be represented in the form of tables and analyzed with the help of descriptive statistics.

RESULTS

This study was carried out in the Department of Obstetrics and Gynaecology of J.L.N. Medical College and Associated Group of Hospitals, Ajmer on 160 pregnant women between 2018 to 2019.

TABLE 1:
DISTRIBUTION OF PATIENTS ACCORDING TO ABO Rh OF HUSBAND

ABO Rh of husband	No. of cases	%
Rh negative husband	32	20
Rh positive husband	128	80
Total	**160**	**100**

Table 1 shows that out of 160 Rh negative mothers 32 (20%) had Rh negative husband and 128 (80%) had Rh positive husbands.

TABLE 2:
DISTRIBUTION OF PATIENTS ACCORDING TO ABO Rh OF BABY

Rh Negative Mother	Rh Negative Baby	Rh Positive Baby
160	34	126
100%	**21.25%**	**78.75%**

Table 2 shows that out of 160 infants 34 (21.25%) were Rh negative and 126 (78.75%) were Rh positive.

TABLE 3:
DISTRIBUTION OF PATIENTS ACCORDING TO PRESENCE OF ERYTHROBALSTOSIS FOETALIS

Gravida	Total	Erythroblastosis foetalis			
		Present		Absent	
		No.	%	No.	%
Primigravida	62	4	2.5	58	36.25
Secondgravida	52	2	1.25	50	31.25
Multigravida	46	4	2.5	42	26.25
Total	**160**	**10**	**6.25**	**150**	**93.75**

Table 3 shows that out of total 160 babies of Rh negative mothers, 10 babies (6.25%) had erythroblastosis foetails. Out of these 10 erythroblastotic babies, 4 (2.5%) belonged to primigravidae, 2 (1.25%) belonged to second gravid and 4 (2.5%) belonged to multigravida. Babies of 58 out of 62 primigravida, 50 out of 52 second gravid and 42 out of 46 multigravida patients escaped erythroblastosis.

TABLE 4:
DISTRIBUTION OF PATIENTS ACCORDING TO COMPARISON OF FOETAL OUTCOME IN Rh NEGATIVE PATIENTS WITH Rh POSITIVE HUSBANDS AND WITH Rh NEGATIVE HUSBANDS

Father	Total	Satisfactory outcome	Bad outcome
Rh negative	32	32	-
Rh positive	128	108	20
Total	**160**	**140**	**20**

Table 4 shows that out of 160 Rh negative patients, 128 had Rh positive husbands. Out of these 128 patients the fetal outcome was satisfactory, i.e. foetuses were not compromised in 108 (67.5%) and foetuses were compromised in 20 (15.6%). 32 Rh negative patients had Rh negative husband and all had good fetal outcome.

DISCUSSION

The foetus inherits its genetic component equally from both parents. Therefore the blood group of the foetus may be different from that of its mother. The foetal red blood cells may thus carry antigens which are foreign to the mother. Leakage of foetal red cells into the maternal circulation in sufficient amount may provoke an antibody response in the mother. These antibodies after crossing the placenta react with antigens on foetal RBCs and cause haemolysis and progressive anaemia, which stimulate erythroblastosis. The majority of these manifestations are due to rhesus incompatibility but ABO and other minor blood groups are occasional offenders.

In this study we have assessed the foetal outcome in 160 Rh negative mothers, who were sensitized as well as who were not sensitized. Assessment has been done by determining the ABO and Rh blood group of the patient and her husband and the Rh antibody titre of the patient at 28 weeks and 36 weeks of gestation.

Assessment of the baby was done by determining the ABO and Rh, Hb% and serum bilirubin of the cord blood at birth.

The serum bilirubin of babies on a higher level at birth was repeated after 24 hours. A gross general examination of the baby was done at birth to note congenital anaemia, icterus and features of erythroblastosis foetalis.

Out of 160 Rh negative patients 32 (20%) had Rh negative husband and 128 (80%) had Rh positive husbands. The 32 Rh compatible matings (irrespective of ABO compatibility), resulted in infants having Rh negative blood group.

There were 34 Rh negative infants, 32 of whom had Rh negative mother and Rh negative father. One Rh negative infant had Rh negative mother and Rh positive father. This may be contributed to the fact that Rh positive individuals may be homozygous for the D antigen or heterozygous for it. If the husband is Rh positive heterozygous (Dd), then 50% of his genes will be transmitted to the offspring as Rh negative. Since the mother is Rh negative, the baby will be Rh negative.

Out of 160 Rh negative women, the babies of 26 (16.2%) mothers were affected by Rh isoimmunization. The fathers of 26 of these isoimmunized babies were Rh positive.

ABO compatibility – 14 out of 26 couple were ABO compatible and 6 were ABO incompatible. According to Hanlon – Lundberg. Kathleen M in December 2000, ABO incompatibility usually does not adversely affect the neonatal outcome.

Out of 160 study group 126 babies were Rh positive. Out of these 126 babies 26 were severely affected. In the 26 severely affected babies the weight ranged from 900 g to 4 kg. 46 out of 132 affected babies had weights ranging from 1 kg to 3 kg. 14 babies showed macrosomia due to Rh incompatibility; however majority of the affected babies showed average weight at birth.

In the present study it was found that 52 isoimmunized babies had congenital anaemia with Hb% ranging from the lowest of 7.6% in 4 baby, 8 g% in 6 babies, 9-10 g% in 14 baby and the rest ranging between 10 g% to 12 g% in 28 babies.

This can be explained by the fact that Rh antibodies are capable of crossing the placenta and on entering the fetal circulation, they react with antigens on fetal RBC's and cause hemolysis and progressive anaemia. The fetus responds to meet this jeopardy of enhanced breakdown of its blood cells by stimulating erythroblastosis.

Icterus was invariably present in all babies of which 16 were moderately icteric with serum bilibrubin of the order of 10 g/dl to 15 g/dl at birth and 14 were severely icteric with serum bilirubin ranging from 16.8 to 18.6 mg/dl.

There were 10 babies in whom the serum bilirubin was on the higher side at birth and hence bilirubin was repeated after 24 hours of birth. 16 foetuses were IUDs and serum bilirubin could not be repeated at 24 hours.

In 8 babies the rise in serum bilirubin level after 24 hours was of the order of 2.2 to 2.6 mg/dl :-

i) The baby with a rise of 2.6 mg/dl in the serum bilirubin was severely icteric, the Hb% was 12 g% and placental weight was 0.86 kg. ET was given with double volume to the baby in nursery, and after the transfusion baby was handed over to the mother. Thus exchange transfusion has very good results and is very effective in reversing the effects of Rh isoimmunisation.
ii) The baby with a rise of 2.2 mg/dl in serum bilirubin was Rh negative. The weight of the baby was 1.7 kg and congenital anaemia was present (10g%). The serum bilirubin at birth was 12.2 mg/dl. The features of erythroblastosis foetalis were absent and weight of placenta was 0.56 kg. The affection of baby can be attributed to minor blood group antigens such as C, Kell, E. C. F_y^a, C. The antibodies to these may cause severe alloimmunization and erythroblastosis as that caused by anti D antibodies.
iii) In 26 babies the rise in serum bilirubin was below 1 mg/dl and these babies survived.

Hence it can be concluded that level of serum bilirubin at birth is not the only criteria for good or bad foetal outcome. It is the fully equipped neonatal care unit and good paediatric care which plays an important role in the good neonatal outcome.

In my study group, the placental weight varied from 0.36 kgs to 0.9 kg. In 96 cases the placental weight was in the normal range i.e. 0.41-0.6 kg. In other 22 cases, the placental weight was between 0.61-0.8 kg. In 6 cases the placental weight was from more than 0.81-0.9 kg. Thus placentomegaly was observed in 28 cases. Out of these 28 cases 20 babies were alive and 8 were IUDs.

In our study the Rh antibody titre was found positive at 28 weeks in 8 patients and were of the order of 1:4 to 1:8 dilutions. These patients were given 300 µg of anti D during the antenatal period.

At 36 weeks, 22 patients had positive Rh antibody titre. Out of these 22 patients 12 had titre positive in 1:4 dilutions which does not signify Rh sensitization. All of these patients had normal babies.

Four patients had Rh antibody titre of 1:8 dilution at 36 weeks. The babies of one of these patients was icteric with serum bilirubin of 12.0 mg/dl and 12.3 mg/dl at birth and after 24 hours, respectively. The other baby had serum bilirubin of 1.1 mg/dl at birth. Both of these babies survived.

Two unbooked patient had Rh antibody titre of 1:32 at 36 weeks. The serum bilirubin of baby was 17.9 mg/dl at birth and 20.5 mg/dl after 24 hours. The baby was given exchange transfusions and ultimately shifted to the mother in good condition.

Four patients had titre of 1:64 at 36 weeks and all were IUDs. These patients had come as unbooked cases.

Hence it was observed that of all the Rh positive babies of Rh negative mothers, some had macrosomia, congenital anaemia, raised serum bilirubin levels and placentomegaly. All of these babies survives due to good antenatal management, intranatal precautions and post natal care of the neonates. All the IUD cases had come as unbooked cases.

CONCLUSION

In this study it was observed that all those patients though severely affected had good foetal outcome due to safe and proper delivery practise in the institution and prompt management of the newborn. As results all the neonates all the neonates survived except those who had come as IUDs. So it can be concluded that the importance of antenatal supervision cannot be overemphasized. The antenatal supervision and timely management of any complication in a pregnant woman is the main objective of the MCH and RCH services of the Government of India. Simple tests such as ABORh grouping of patients and her husband at the first antenatal visit is very important and helpful for better outcome of pregnancy. If required the Rh antibody titre at 28 weeks 36 weeks should be done as it is very important regarding the further management of an Rh immunized pregnancy. It can be further stressed that simple measures of safe delivery practices and prompt and intensive care of the neonate can reduce the perinatal morbidity and mortality due to Rh incompatibility, in our country were we are having

shortage and constraints of facilities.

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