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MATERNAL AND FETAL OUTCOME IN RH NEGATIVE PREGNANCY

Dr Uma Jain*	Professor, Dept. Of Obstetrics & Gynaecology, GMC Associated With DH Shivpuri, (M.P.) India. *Corresponding Author
Dr Preeti Gupta	Senior Consultant, Dept. Of Obstetrics & Gynaecology, Gupta Hospital, Morar Gwalior, M.P. India.
Dr Deepa Gupta	MS, (OBGY) DND, MNAMS, FICMCH Consultant, Obstetrician & Gynaecologist And Infertility Specialist Sree Krishna Medical And Research Center Delhi Ex Asst Prof MGMC Indore M.P. India.
Dr Deepali Jain	Senior Resident Department Of Obstetrics & Gynaecology, GMC Shivpuri M.P. India.

ABSTRACT **INTRODUCTION-** When Rh negative maternal blood is exposed to Rh positive fetal blood (RBC) in maternal circulation, antibodies against Rh (D) may develop in the mother. These Rh (D) antibody, once produced, remains in the woman's circulation and poses the threat of hemolytic disease (due to destruction of fetal RBCs) for subsequent Rh-positive fetuses and this event leads to alloimmunization. Coombs test is the most common method to detect alloimmunization done during pregnancy (ICT) and in postnatal period (DCT). Rhesus (Rh) isoimmunization is an important clinical entity in India and other developing countries, which is responsible for fetal anemia and hydrops fetalis, and if not treated, it can result in intrauterine fetal demise, thus timely diagnosis follow-up and management of Rh –ve pregnancy is must.

MATERIAL AND METHODS- This is a retrospective observational study, done in a private hospital, Gwalior (M.P.), form 1st Jan. 2018 to 30th June 2020. 88 women with Rh-ve pregnancy were studied during this period, Data was recovered from labor room record, OT, PNC, post operative wards for maternal outcome a SNCU for neonatal outcome.

RESULTS- In our study the most common age group was 21-25 years (62.5%), most of the patient were Primigravida(42.4%), most of them were unbooked (65.90%) and from Rural area (72.72%).
The most common blood group Rh- was o-ve (53.40%).
Only 2 patients had positive indirect coombs test.
Most of the patients delivered normally, only (28.40%)Patients delivered by LSCS.
Preeclampsia was the most common maternal complication found in Rh- Patient (12.5%).
96.59% of Neonates were live born. 2.27% were fresh still born and 1.13% were macerated still born.
24 babies were admitted in SNCU. The most common cause of admission was neonatal jaundice (66.66%).
The most (76.13%) of the babies had serum bilirubin level between 10-15 mg/dl.

CONCLUSION- We concluded that Rh isoimmunization leads to increased perinatal morbidity for perinatal morbidity. The obstetrician and maternity staff should be familiar to diagnosis and management of with Rhesus incompatibility and they should counsel the Rh negative patient about Importance of checking blood group and Rh type in pregnancy and should educated them about importance of Rh prophylaxis and Hemolytic diseases of fetus and newborn risks of present and future pregnancy. During past few decades there had been major advances in the medical treatment for Rh negative pregnancy.

KEYWORDS : alloimmunization, fetal anemia, fetal hydrops

1. INTRODUCTION-

Rhesus (Rh) isoimmunization occurs in approximately 1 per 1000 births in Rh negative women.[1]

When Rh negative maternal blood is exposed to Rh positive fetal blood (RBC) in maternal circulation, antibodies against Rh (D) may develop in the mother. These fetal red cells can enter her circulation during small fetomaternal bleeding episodes in the early third trimester or during delivery, abortion, ectopic pregnancy, abruptio placentae, cesarean section, or other instances of antepartum bleeding (obstetric procedures Amniocentesis, Chorionic villus sampling, Cordocentesis, External cephalic version, manual removal of placenta). These Rh (D) antibody, once produced, remains in the woman's circulation and poses the threat of hemolytic disease (due to destruction of fetal RBCs) for subsequent Rh-positive fetuses and this event leads to all oimmunization. Coombs test is the most common method to detect alloimmunization done during pregnancy (ICT) and in postnatal period (DCT)[2].

Fetomaternal hemorrhage can be detected through Kleihauer Betke test, Flow Cytometry and Rosetting test.

Maternal effect of Rh negative pregnancy are increase incidence of Pre-eclampsia, Polyhydramnios, Coagulopathy (If fetus is dead), Postpartum hemorrhage (secondary to coagulopathy, polyhydramnios and placentamegaly)[3].

Rhesus (Rh) isoimmunization is an important clinical entity in India and other developing countries, which is responsible for fetal anemia and hydrops fetalis, and if not treated, it can result in intrauterine fetal demise. Rh isoimmunization is responsible for severe jaundice in neonates, which can be severe enough to cause kernicterus with debilitation consequences, if not treated adequately. It can be prevented with simple measures and treated if recognized in time. Thus severity of hemolytic disease of the fetus and new born, can have variety of manifestations mild- Congenital anemia of the newborn (45-50%), Moderate: Icterus gravis neonatorum (25-30%) and Severe : Hydrops fetalis (20-25%)[1].

Ultrasound is useful in management of Rh alloimmunized pregnancy though it helps in assessment of fetal growth, Identify hydrops/fetal ascites/cardiomegaly/hepatosplenomegaly/pleural or pericardial effusion, detect fetal anemia using middle cerebral, umbilical vein and ductus venous Doppler studies. Liquor abnormalities like poly/oligohydramnios, Placental thickness and Fetal anasarca can be seen by ultrasound.[3,4]

Managements of Rh negative woman with Rh positive Husband depends upon whether patients is alloimmunized or not[1,3,5,6].

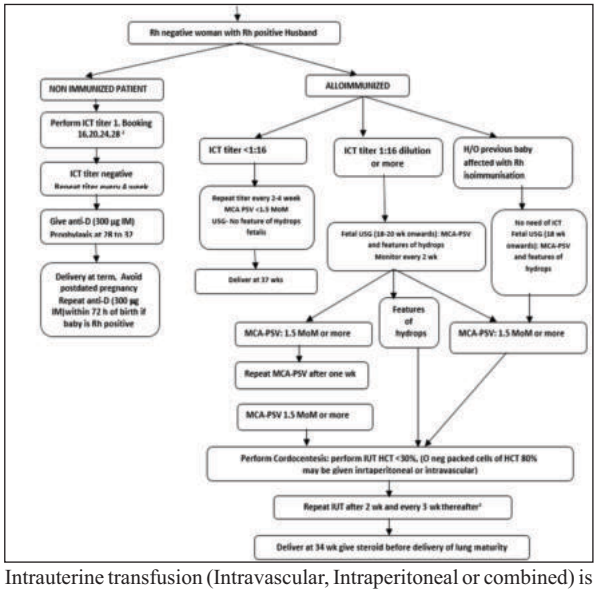
1. NON IMMUNIZED PATIENT -ICT titer negative
2. ALLOIMMUNIZED
- ICT titer <1:16
- ICT titer 1:16 dilution or more
- H/O previous baby affected with Rh isoimmunisation

Fetal Doppler MCA-PSV (fetal middle cerebral artery peak systolic velocity) index (developed by **moise et. al.**) is used to monitor alloimmunized mother.

Monitoring of MCA-PSV should be started in patients with risk of fetal anemia from 18-20 weeks gestation and when the titer above critical level (ICT titer 1:16 dilution or more) is. The antibody titers are repeated between 2-4 weeks depending on other risk factors. If the

titer has increased rapidly or the patient has had a previous pregnancy affected by Rh isoimmunisation we would recommend reassessing 2 weekly. If the MCA-PSV remains below 1.5 MoM we follow the patient up with serial MCA-PSV estimations until 35 weeks, administer steroids for fetal lung maturity and then consider delivery at 36-37 weeks[1, 3, 7] Management of all types of Rh negative patients is presented in flowchart.

Flowchart 1- Management of Rh negative pregnancy[1,3,5].



Intrauterine transfusion (Intravascular, Intraperitoneal or combined) is indicated if (Before 26 weeks gestation-hematocerit <25%, After 26 weeks gestation-hematocrit <30%)[3].

Passive immunization against hemolytic disease of the newborn is achieved with Rh (D) immune globulin, a purified concentrate of antibodies against Rh, (D) antigen. The Rh (D) immune globulin (one vial of 300 mcg intra muscularly) is given to the mother within 72 hours after delivery (or spontaneous or induced abortion or ectopic pregnancy). The antibodies in the immunoglobulin destroy fetal Rh-positive cells so that the mother will not produce anti-Rh (D). During her next Rh-positive gestation, erythroblastosis will be prevented. An additional safety measure is the routine administration of the immunoglobulin at the 28th week of pregnancy. the passive antibody titer that results is too low to significantly affect an Rh-positive fetus. the maternal clearance of the globulin is slow enough so that protection will continue for 12 weeks. Once a woman is alloimmunized, Rh (D) immune globulin is no longer helpful and should not be given[2,8].

Rh negative woman if delivers a Rh positive ABO compatible infant has a likelihood of isoimmunization of 16% (2% at time of first delivery, 7% will have Anti Rh D antibody 6 months post partum, 7% will Manifest early in 2 pregnancy[9].

They should be educated about timely visit to hospital and advised for delivery at higher centre where facility of fetal monitoring ,intrauterine transfusion and exchange transfusion should be available and under multidisciplinary approach.

Counseling of parents regarding the neonate and also about the next pregnancy should form a part of ideal management.

Ultrasonography was done to know the USG was repeated at regular intervals as per need.

2. MATERIAL AND METHODS

This is a retrospective observational study, done in a private hospital, Gwalior (M.P.), form 1st Jan. 2018 to 30th June 2020. 88 women with Rh-ve pregnancy were studied during this period, Data was recovered from labor room record, OT, PNC, post operative wards for maternal outcome a SNCU for neonatal outcome.

Various information were collected like age, parity, residence, previous obstetric history, family history, blood group of the husband or her previous child, ICT test, h/o Anti-D prophylaxis given in present or in previous pregnancy, ultrasound findings (The gestational age, fetal wellbeing, amount of liquor, placental grading maturation, Middle cerebral artery PSV (MCA PSV if indicated) and any congenital malformations) any maternal complication accompanying, mode of delivery, baby blood group, the neonatal outcome & newborn admitted in SNCU were received for the cause of admission & their severity of jaundice by looking into the level of their s bilirubin.

All the data were analyzed using IBM, SPSS Ver. 20 software. Cross Tabulation and frequency distribution were used to prepare tables. Data are expressed as numbers, percentages, and mean.

3. RESULTS

In our study total deliveries from 1st Jan. 2018 to 30th June 2020 were 2140 and during this period 88 Rh-ve women were delivered in our center hence **the prevalence was 4.11%.**

Other results are as following.

Table 1:- Demographic Profile of study population.

Age in years	Numbers of Cases	Percentage
15-20	19	21.59
21-25	55	62.5
26-30	11	12.5
>30 years	3	3.40
Total	**88**	**100**
Parity		
Primigravidas	37	42.04
Gravida-2	29	32.95
Gravida-3	16	18.18
>G4	6	6.81
Total	**88**	**100**
Booked	30	34.09
Unbooked	58	65.90
Total	**88**	**100**
Residence		
Rural	64	72.72
Urban	24	27.27
Total	**88**	**100**

In our study the most common age group was 21-25 years (62.5%), most of the patient were Primigravida(42.4%), most of them were unbooked (65.90%) and from Rural area (72.72%).

Table 2:- Blood group distribution of Rh- Mother.

Blood Group	Number of Cases	Percentage
A-Ve	15	17.04
B-Ve	22	25
AB-Ve	4	4.54
O-Ve	47	53.40
Total	**88**	**100**

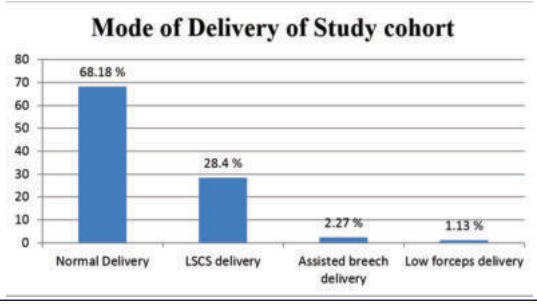
The most common blood group Rh- was o-ve (53.40%).

Table 3:- Result of Indirect Coombs test.(Sensitization of Mothers).

I.C.T.	Numbers of Cases	Percentage
Negative	86	97.72
Positive	2	2.27
Total	**88**	100
Distribution of Cases by Indirect Coombs Test (I.C.T.)		

Most of the patients had negative indirect Coombs test (97.72%). only 2 patients had positive indirect coombs test.

Fig 1:- Mode of Delivery of Study cohort



In our study most of the patients deliver normally only (28.40%) patient delivered by LSCS.

Table 4:- Maternal outcome in Rh negative patients.

Associating factors	No. of patients	Percentage
PIH/preeclampsia	11	12.5
Abruption placentae	4	4.54
Oligohydrmnios	4	4.54
Polyhydramnios	2	2.27
Total	**21**	**23.86**

Preeclampsia was the most common maternal complication founding in Rh- Patient (12.5%).

Table 5:- Neonatal Outcoming Rh- Pregnancy.

Neonatal Outcome	Numbers of Cases	Percentage
Live born	85	96.59
Fresh stillbirth	2	2.27
Macerated stillbirth	1	1.13
Total	**88**	**100**

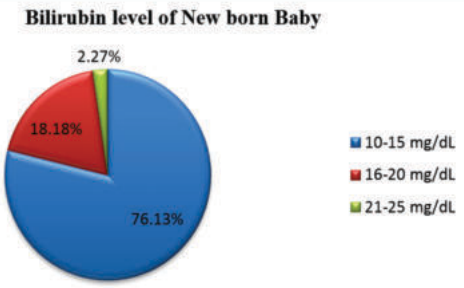
96.59% of Neonates were live born. 2.27% were fresh still born and 1.13% were macerated still born.

Table 6:- Cause of Admission of Newborn baby.

Cause of Admission	Numbers in Cases	Percentage
Neonatal Jaundice	16	66.66
Meconium Aspiration Syndrome	2	8.33
Sepsis	1	4.16
Respiration Distress Syndrome (RDS)	2	8.33
Prematurity	2	8.33
Others	1	4.16
Total	**24**	**100**

24 babies were admitted in SNCU. The most common cause of admission was neonatal jaundice (66.66%).

Fig 2:- Bilirubin level of New born Baby.



The most (76.13%) of the babies has serum bilirubin level between 10-15 mg/dl.

4. DISCUSSION:

In this study, we observed the number of deliveries that took place between the time span of 1st Jan. 2018 to 30th June 2020. A total of 2140 deliveries were observed. Out of which 88 women were Rh negative. So the prevalence of Rh negative factor in our study was 4.11%. A study conducted by **Singh A et al** [10] showed that prevalence of Rh negative factor was 1.43%. Another study done by **Mondal B et al**[11] concluded that Rh negative prevalence was 2.3%. Many other studies conducted by **Nagamuthu et al**[12], **Okeke TC et al**[13], **Khatun J and Begum R et al**[14], **Devi G R et al**[15] had prevalence of 4.29%, 4.50%, 2.83% and 4.26%, all the findings are in accordance with our study.

Out of 88 women, 19 (21.59%) women belonged to the age group of 15 to 20 years. 55 (62.5%) women were of age group 21 to 25 years. 11 women (12.5%) belonged to age group lying between 26 to 30 years and only 3 women(3.40%) were above 30 years of age. In our study the most common age group was 21 to 25 years. **Pinapothu et al**[16] reported that the highest incidence was found in age group 23-26 years (41.5%) in year 2018-19 while in year 2008-09 highest incidence was in age group 18-22(45.5%) and >30 years 4.6% and 3.4% respectively.

Most of the women in our study were primigravida (42.04%), followed by gravida- 2 (32.9%), gravida- 3 (18.18%) and >gravida 4 (6.8%). A study was conducted by **Pinapothu et al**[16] in 2019. They also reported in their study that primigravida showed highest distribution i.e. 50.3% and 52.3% in year 2018- 19 and 2008-09 respectively. These findings were similar to our study.

Out of the total participants, 58 women (65.90%) were unbooked and 30 women (34.09%) were booked. Most of the women (64%) belonged to rural areas and only 24% belonged to urban areas. In studies conducted by **Alakananda et al**[17] (2016) also showed 60% cases were unbooked. And studies conducted by **Aljuhaysh RM et al**[18] (2017) and **Joseph et al**[19] (2017) also showed that 55% cases and 74% cases were unbooked. Thus unbooked cases were more common in the studies which highlights the situation of unawareness in our society.

In our study, it was observed that the most common blood group of the mother was O-ve (53.40%), followed by B-ve (25%), A-ve (17.04%) and AB-ve (4.54%). A study done by **Kanko et al**[20] showed that 159 (38.1%) of the total study participants were found to be of blood group O-ve. The next highest group was A with 119 (28.5%). This study revealed that 2.1%, 1.9%, 1.2%, and 1% of the study population with blood groups O, A, B, and AB were Rh D negative, respectively.

86 patients in our study had negative Indirect Coombs test (97.7%) and only 2 patients (2.27%) had positive Indirect coombs test. Studies done by **Devi GR et al**[15] (2016) and **Agrawal et al**[21] (2016) also showed similar results where 4% and 5% cases respectively were sensitized.

This study highlighted that 60 patients (68.18%) had normal delivery. 25 women (28.4%) had LSCS delivery. Only 2 women (2.27%) had assisted breech delivery and 1 woman (1.13%) had low forceps delivery. Study done by **Sreelatha et al**[22] in 2017 showed 294 (56.4%) vaginal deliveries and 430 (43.5%) cases of caesarean section whereas there were 44 (46.3%) vaginal and 51 (53.7%) caesarean deliveries in their study; and O-negative was the most common blood group in this study similar to ours.

Our study indicated that 21 women had associated complications, most common, 11 cases (12.5%) being preeclampsia, followed by abruption placentae and oligohydramnios, 4 cases each (4.54%), least common being polyhydramnios, 2 cases (2.27%). In a study done by **Tripathi R et al**[23] eight cases were associated with PIH/preeclampsia, one associated with polyhydramnios and three had abruptio placentae which is similar to our study

Out of 88 women, 85 (96.5%) women gave birth to a live baby. 2 women (2.27%) had fresh stillbirth and 1 woman (1.13%) had macerated stillbirth. The most common cause of admission in SNCU was neonatal jaundice (66.6%). Other causes were meconium aspiration syndrome (8.33%) respiration distress syndrome (8.33%) and prematurity (8.33%). Least common cause was sepsis (4.16%). This finding goes in accordance with **Alakananda et al**[17] where the main cause of admission to NICU was neonatal jaundice (55%).

In our study, we also observed the bilirubin level of the new born baby and concluded that 67 babies (76.13%) had bilirubin lying in the range of 10- 15 mg/dl. 16 babies (18.18%) had bilirubin of range 16 – 20 mg/dl and only 2 babies (2.27%) had bilirubin lying in the range of 21-25 mg/dl. In a study conducted by **Tripathi R et al** [23] , the results showed serum bilirubin in 48 babies was <2.8 mg%; 1 had level between 2.8-4.0mg% and 6 babies had level >4.0 mg%.

5. CONCLUSION

The obstetrician, maternity nurse, and the labor & delivery nurse should all be familiar to diagnosis and management with Rhesus incompatibility and they should counsel the Rh negative patient about Importance of checking blood group and Rh type in each pregnancy and should educated them about importance of Rh prophylaxis and Hemolytic diseases of fetus and newborn risks of future pregnancy.

During past few decades there had been major advances in the medical treatment for Rh negative pregnancy.

NIPT (cell-free DNA), MCA-PSV monitoring, early detection of antibody titer, intra uterine transfusion & intra venous immunoglobulin, etc have made monitoring the pregnancy case & prevention and treatment of neonatal morbidity and mortality accessible.

The major drawback is seen in the high cost of RAADP [Anti-D prophylaxis] owing to high cost & these recent technologies are available only at higher centers.

Also the post procedure prophylaxis (after MTP, abortion, ectopic pregnancy etc) needs to be rigorously implemented.

FUTURE-

Although modern imaging techniques, fetal blood sampling an intrauterine blood transfusion are available, but they are no without hazards. Therefore we must think of alternative concepts. Anti-D prophylaxis is needed but reserves of immunoglobulin are very limited. Hence, there is a need for synthetic antibody.

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