To Evaluate the Etiological Determinants of Rhesus Isoimmunization and to Study Its Perinatal Outcome

NEETU SINGH*, KIRAN PANDEY†, PREETI DUBEY‡, YASHWANT RAO#

ABSTRACT

Aims and objectives: To evaluate the etiological determinants of Rhesus (Rh)-immunization and to study the prevalence of perinatal mortality and morbidity in Rh-immunization. **Material and methods:** This retrospective study was carried out in the Dept. of Obstetrics and Gynecology, UISEMH, Kanpur from November 2007 to November 2010. All cases were thoroughly studied specially their history, examination, investigation, mode of delivery, passive immunization and their perinatal outcome. **Results:** We found an increased rate of isoimmunization with increasing parity. Most of our patients were gravida 4 (44%). In our study, we found that 84% of isoimmunized patients had a history of previous delivery in which there must have been a large fetomaternal hemorrhage (FMH). It was found that 80% did not receive ante-D while 20% received. Rh-immunization in 20% of those who received ante-D could be explained due to inadequate dosage. The major cause of perinatal morbidity was hyperbilirubinemia followed by anemia. **Conclusion:** Rh-immunization is a persistent problem in developing countries. As Rh-immunizing stimulus occurs late in pregnancy and most often at delivery, a successful program for Rh immunoprophylaxis with Rh-Ig, prevents not only fetal death but also sensitizing prospects. Early reference of affected patients with early assessment and judicial interventions as well as intensive neonatal care is essential in ensuring satisfactory results.

Keywords: Rhesus (Rh)-immunization, isoimmunization, perinatal outcome, Rh-Ig, Rh immunoprophylaxis, intensive neonatal care

About 5-10% of Indian population is Rhesus (Rh)-negative. The Rh gene is located on short-arm of chromosome-1. *In utero*, the Rh-antigen is well-developed by Day 38. Rh-immunization is a major problem in developing countries like India.

Rh-stimulus occurs late in the course of pregnancy mostly at the time of delivery. It should be kept in mind that 1-2% of Rh-negative mothers become sensitized to the Rh-antigen during pregnancy by what is known as "silent bleeds". There are many causes of Rh-immunization such as fetomaternal hemorrhage (FMH) during delivery, medical termination of pregnancy (MTP), abruption, placenta previa (PP), bleeding in first trimester, external cephalic version, etc. So, in present day practice, utilization of antibody-mediated immune-suppression in order to assure a more effective disappearance of Rh-disease, is needed and will require a timely antepartum and postpartum prophylaxis to reduce perinatal morbidity and mortality. The relationship between hemolytic disease of newborn (HDN) and Rh-sensitization is well-established by Levine et al in 1941.

An approach to prevention and eradication of this disease has been developed by techniques of preventing immunization in mothers. The development of real time ultrasound and Doppler not only helped us to understand fetal anatomy but also physiological states and dynamics of blood flow in fetal circulation.

Intrauterine transfusion have become routine to treat fetal anemia. Several recent improvements like phototherapy, fibro-optic delivery system and IV-IG have revolutionized the management of hemolytic disease of newborn. Anti-D prophylaxis has been a remarkable step to prevent Rh-immunization. Despite such progress in prevention, Rh-immunization is still widespread. Cases of Rh-immunization are still occurring at an increased rate in India and this urgently calls for re-evaluation of the cases of anti-D prophylaxis.

*Assistant Professor
†Professor and Head
‡Professor
Dept. of Obstetrics and Gynecology
#Assistant Professor
Dept. of Pediatrics
GSVM Medical College, Kanpur, Uttar Pradesh
Address for correspondence
Dr Neetu Singh
Assistant Professor
Dept. of Obstetrics and Gynecology
GSVM Medical College Campus, Kanpur, Uttar Pradesh
E-mail: drneetusingh73@gmail.com

Table 1. Demographic Profile of Rh-immunized Pregnancies

Age in years	No. of cases/ (Percentage) (n = 96)	Parity	No. of cases/ (Percentage) (n = 96)	GA	Incidence of babies affected (n = 86)
<20	1 (1%)	G1	1 (1%)	<34 weeks	24 (28%)
21-25	21 (22%)	G2	13 (14%)	34-37 weeks	20 (24%)
26-30	61 (64%)	G3	15 (16%)	37-40 weeks	37 (42%)
31-35	10 (10%)	G4	43 (44%)	>40 weeks	05 (06%)
36-40	2 (2%)	G5	18 (19%)	Excluding IUD	
>40	1 (1%)	G6	6 (6%)		

AIMS AND OBJECTIVES

To evaluate the etiological determinates of Rh-immunization and to study the prevalence of perinatal mortality and morbidity in Rh-immunization.

MATERIAL AND METHODS

This retrospective study was carried out on 96 patients in the Dept. of Obstetrics and Gynecology, UISEMH, GSVM Medical College, Kanpur from November 2007 to November 2010. All cases were thoroughly studied specially their history, examination, investigation, mode of delivery, passive immunization and their perinatal outcome.

OBSERVATIONS

During 3 years study period, 7920 deliveries occurred in UISEMH. Out of 7,920 deliveries, 560 patients were Rh-negative; giving an incidence of 7%. Out of 560 Rh-negative women, 96 were isoimmunized patients according to their Coomb's titer status. In these 96 cases; 69 women (72%) were unbooked, while 27 women (28%) were booked.

Table 1 shows that maximum women were in the age group 26-30 years (64%). We found an increased rate of isoimmunization with increasing parity. Most of our patients were gravida 4 (44%). It also shows the correlation of outcome of the babies with their respective gestational age. Our study showed that 90% of the preterm babies required treatment while only 27% of term babies required treatment reflecting that preterm babies are more susceptible.

Table 2 shows the etiological determinants. In our study, we found that 84% of isoimmunized patients had a history of previous delivery in which there must have been a large FMH; 10% had a history of antepartum hemorrhage (APH) (abruption - 6%; PP - 4%).

Table 2. To Evaluate the Etiological Determinants of FMH Leading to Rh-immunization

Sensitizing events	No. of cases (n = 96)	Percentage (%)
Bleeding in first trimester	1	1
MTP	4	3
Abortion	1	1
Ectopic	Nil	Nil
H. mole	Nil	Nil
Abruption	5	6
PP with bleeding	4	4
ECV	1	1
Delivery	81	84

Table 3. Association of Mode of Delivery of Previous Pregnancy with FMH

Mode of delivery	Incidence (n = 81)	Percentage (%)
Normal	16	20
Forceps	10	12
Ventouse	8	10
LSCS	18	22
Breech	15	19
IUD	14	17

Table 3 shows that out of those; 58% were complicated deliveries and 22% had a history of cesarean; 20% of patients who had a normal delivery also had FMH.

Table 4 shows relation of isoimmunization with history of anti-D received, it was found that 80% did not receive ante-D, while 20% received. Rh-immunization in 20% of those who received ante-D could be explained due to inadequate dosage.

Table 5 shows the clinical outcome; 45% had hyperbilirubinemia, 28% were anemic while

Table 4. History of Anti-D Received

Received	20%
Not received	80%

Table 5. Clinical Outcome of Rh-positive Babies

Clinical outcome	No. of cases	Percentage (%)
Hyperbilirubinemia	43	45
Anemia	27	28
Kernicterus	8	8
Hypoglycemia	6	7
Hydrops-fetalis	2	2
IUD	10	10

Table 6. Perinatal Outcome in Rh-sensitized Pregnancies

Perinatal outcome	No. of cases	Percentage (%)
NICU admission		
Expired	11	12
Recovered	36	38
IUD	10	10
No treatment required	39	40

kernicterus, hypoglycemia, hydrops and intrauterine device (IUD) were found in 8%, 7%, 2% and 10% cases, respectively. The major causes of perinatal morbidity were hyperbilirubinemia followed by anemia.

Table 6 shows perinatal outcome 40% required no treatment while 50% required treatment out of which 12% expired. Recovery was noted in 38% of cases.

DISCUSSION

One would expect the incidence of Rh-immunization to be low but this does not appear to be the case due to lack of ante-D prophylaxis and inadequate dosage of anti-D given after delivery. Therefore, the exact incidence is probably unknown due to failure to diagnose or under reporting as stated by Mandeep et al. The prevalence of Rh-immunization in our study was 15% out of those who were Rh-negative.

According to Lau et al (1995) external cephalic version (ECV) caused FMH in 2-6% cases, though in our study only 1% had a history of ECV. Reddy et al (1999), reported incidence of FMH in first, second and third trimester as 6.7%, 13.9% and 29%, which was similar in our study which reported the incidence of 4.5%, 9.5% in first and second trimester. In our study, majority (84%) of the patients who were isoimmunized had a previous history of delivery.

Bowman et al (1988) evaluated and found that FMH occurred at delivery in 90% and antenatally in 10%; in concordance to his study 84% of patients had history of delivery, while 16% cases were associated with antenatal FMH in our study. In one case, primigravida was noted to be isoimmunized. After a proper evaluation, she had no history of any FMH or any blood transfusion. This may be explained by silent FMH occurring throughout pregnancy. Frigolette et al (1983) showed in his study that 1-2% of cases may have FMH known as "silent bleeds".

The majority of the cases were having no history anti-D after delivery (80%), it was found that 60% patients with previous history of complicated vaginal delivery and cesarean section had large amount of FMH leading to isoimmunization. This was supported by Mehta et al (1979) who showed that complicated or instrumental deliveries increase the risk of FMH to around 80%.

Rh-immunization causes significant perinatal mortality and morbidity; this was shown by Diamond et al (1932) and Levine et al (1941).

The clinical outcome varied, out of which the most common morbidity was hyperbilirubinemia followed by anemia. Our study reported a perinatal mortality of 22% (including IUD) and perinatal morbidity of 38%. Higher perinatal mortality in our study may be due to 72% of unbooked cases, which did not receive any antenatal care and were referred to our tertiary care center with antepartum and intrapartum complications.

Our results for perinatal morbidity shows that 40% required no treatment, 38% recovered after treatment, while 22% expired despite treatment due to severe disease. Our outcomes were comparable to Alvin et al (1995) who during their study noted that 51% required no treatment, 31% required treatment after term delivery. Ashma Madan et al (2004) also showed that 25% have severe disease, 20% have no apparent disease.

CONCLUSION

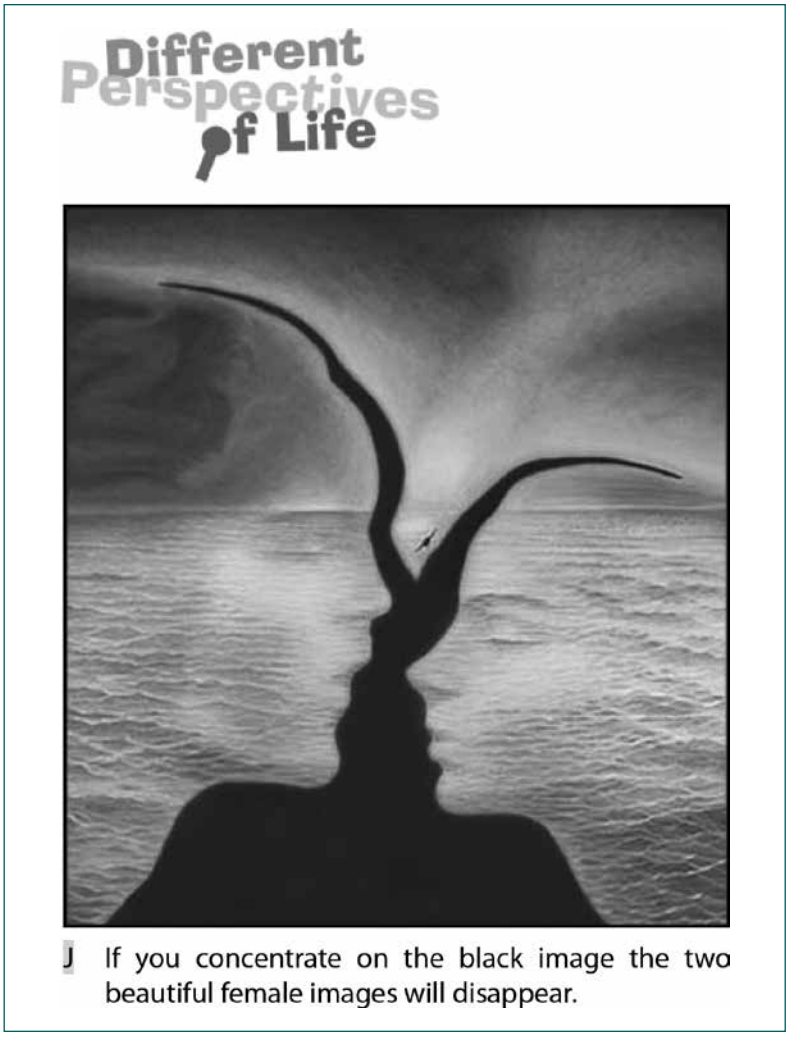
Rh-immunization is a persistent problem in developing countries. As Rh-immunizing stimulus occurs late in pregnancy and most often at delivery, a successful program for Rh immunoprophylaxis with Rh-IgG, prevents not only fetal death but also sensitizing prospects. Early reference of affected patients from periphery to higher center, with early assessment and judicial interventions as well as intensive neonatal care are essential in ensuring satisfactory results.

Future challenges such as spreading awareness of the need of antenatal prophylaxis, routine postpartum prophylaxis is to be emphasized. Advanced method for increasing safety of anti-D preparations, use of monoclonal Rh-D antibodies and newer future test for FMH will need future researches.

SUGGESTED READING

1. Alvin: Avery's Textbook of Neonatology, Isoimmune HD. Alvin Zipursky, John M, Bowman; 1995. pp. 44-66.
2. Neonatal Hyperbilirubinemia (Chapter 79). Asthma Avery's Textbook of Neonatology. 8th Edition, 2004. p. 1231.
3. Bowman JM. The prevention of Rh immunization. Transfus Med Rev. 1988;2(3):129-50.
4. Diamond LK, Blackfan KD, Baty JM. Erythroblastosis fetalis and its association with universal oedema of fetus; icterus gravis neonatorum as anaemia of the newborn. J Pediatr. 1932;1(3):269-76.
5. Frigolette FD Jr (Ed.). Antepartum administration of Rh immune globulin: a guide to office procedure. Raritan, NJ: Ortho-Diagnostic Systems, Inc.; 1983.
6. Lau TK, Stock A, Rogers M. Fetomaternal haemorrhage after external cephalic version at term. Aust N Z J Obstet Gynaecol. 1995;35(2):173-4.
7. Levine P, Burnham L, Katzin EM, Vogel P. The role of iso-immunization in the pathogenesis of erythroblastosis fetalis. Am J Obset Gynecol. 1941;42:925-37.
8. Mandeep et al. FOGSI FOCUS. 2006;11.
9. Mehta DM, Gupte SC, Bhatia HM. Transplacental haemorrhage and maternal iso-immunization. J Postgrad Med. 1979;25(2):75-80.
10. Reddy U, Wilter. Isoimmunization. In: Lambrous N, Morse. A Wallach EE (Eds.). John Hopkins Manual of Obstetrics and Gynaecology. Baltimore: Lippincott Williams & Wilkins; 1999. p. 199.

■■■■



J If you concentrate on the black image the two beautiful female images will disappear.