The Frequency and Clinical Profile of Rh D Alloimmunised Pregnancies in a Tertiary Care Centre in Kerala

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ABSTRACT

Introduction: Development of anti D immunoglobulin, Better facilities for early detection and treatment and better neonatal care has brought down the frequency and magnitude of HDFN. But assessment of frequency of Rh D alloimmunisation and HDFN in individual centres is important since it varies depending upon the monitoring facilities and access to health care system.

Aim: To find out the frequency of Rh D alloimmunisation in antenatal cases and frequency of HDFN in their offsprings.

Materials and Methods: Longitudinal cross sectional study done in Department of Transfusion Medicine on 64 antenatal cases positive for anti Rh D antibodies by ICT whose clinical profiles and antibody titres were recorded. Data was analysed in SPSS ver.17

Results: Out of 2496 RhD negative women tested with ICT,78 (3.12%)were positive. Failure to administer RhIg lead to alloimmunisation in 42(65.6%) cases. Frequency of HDFN was 57/ 64 cases. 53 RhD positive newborns were DCT positive (93.1%) and 4 were negative(6.9%). Male: female ratio 1.46:1.

Conclusion: Frequency of Rh D alloimmunisation is higher in the institution compared to global standards and majority are a result of lack of RhIg prophylaxis. Better strategies to prevent RhD alloimmunisation and introduction of interventions like IUT are warranted.

Keywords: Rh D alloimmunisation, RhIg, Hemolytic Disease of Fetus and Newborn, Anti D prophylaxis.

*See End Note for complete author details

INTRODUCTION

Hemolytic disease of Fetus and Newborn due to Rh D alloimmunisation was one of the serious complications of pregnancy a few decades back, which accounted for many cases of perinatal deaths and disabilities. But the development of anti D immunoglobulin has drastically reduced the incidence of Rh D sensitization. Before the establishment of Rh D prophylaxis in 1960s,16% of susceptible antenatal cases developed allo anti D whereas by 1974 it was reduced to<2%.1 After introduction of additional ante partum prophylactic RhIg, the frequency of Rh D alloimmunisation is now well below 0.2%. Better facilities for early detection and treatment of haemolytic disease of fetus and newborn as well as better neonatal care has further contributed to bring down the magnitude of severe HDN. But both these advantages of prompt anti D prophylaxis and efficient neonatal care is obviously limited to places with reasonably good access to health care. Hence it seems prudent for each country especially developing countries like India to have ample number studies from various parts of country including areas with less access to health care.

The Obstetrics and Gynecology wing of Medical college Trivandrum caters not only to inhabitants of Trivandrum and nearby districts but also to southernmost parts of Tamil Nadu. A large number of RhD negative cases are referred from peripheral centres due to issues of blood availability, and for better monitoring of pregnancy and anticipated perinatal problems. Routine antenatal anti D prophylaxis is not established here yet but post partum prophylaxis is efficiently practiced. There have been no studies till date about the magnitude of Rh D sensitisation and HDFN in pregnancies presenting to Medical College Trivandrum. This study reports the frequency of alloimmunisation as well as HDFN in Rh D negative females and their clinical profile which will be the first and essential step before trying to reduce the morbidities of this preventable cause for fetal loss.

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MATERIALS AND METHODS

This is a Longitudinal cross sectional study done on 64 Rh D negative antenatal cases whose blood samples were found positive for anti Rh D antibodies by Indirect Coombs Test. Study was done from 1- 10-2008 to 30-09-2010 in Department of Transfusion Medicine, Govt. Medical College, Trivandrum.

Indirect Coombs Test was done on blood samples of Rh D negative cases during the study period and positive cases were further evaluated. Fresh 10 ml samples were collected from each positive case. Cell and Serum were separated. ABO grouping (forward and reverse) and Rh D typing were done by tube method. Rh D Negative status is confirmed by weak D test. Samples were screened for the presence of anti D antibodies by Indirect Coombs Test by tube method and confirmed by LISS-Coombs gel cards. Demographic data and history of Rh Ig administration, previous pregnancies etc was elicited. Antibody titration was done on ICT $+^{ve}$ samples by tube method. Titre was recorded and serum preserved frozen at -20^{0}C deep freezer for future reference. Antibody was identified as anti D in frozen samples at a later period using 11 cell panel in order to exclude the cases with presence of non-D antibodies .Patients were followed up monthly till 28 weeks and thereafter biweekly. Serial antibody titres were obtained. Blood group, Du testing and Direct Coombs test was done on cord blood sample of the infant.

Inclusion criteria for study subjects were

1. ICT with O Rh D + red cells positive
2. Antibody identification panel pattern shows only Anti D
3. No fetomaternal ABO incompatibility.

All statistical data were analyzed by using SPSS software version 16. Continuous variables were expressed as mean ± standard deviation and qualitative data was expressed as percentage. Independent test was used for comparing quantitative data between groups. Categorical variables were compared using chi square test. All p values were two tailed and values of $p<0.05$ was considered statistically significant.

OBSERVATIONS AND RESULTS

Total number of RH D negative women in whom ICT for anti D antibody was done in Department of Transfusion Medicine from 1-10-2008 TO 30-09-2010 was 2496. Out of these, 78 antenatal cases were found positive for anti D antibodies. 64 cases who satisfied the inclusion criteria were included in the study.

The distribution of study subjects according to Age, parity and order of affected pregnancy is shown in Figure 1 a & b respectively. Table 1 shows the order of affected pregnancy.

Out of 2496 Rh D Negative cases, 78 cases (3.12%) were found to be alloimmunised.64 cases were included. Youngest in the study group was of 18 yrs and eldest was of 42 yrs. Majority (45.31%) of alloimmunised women were of age group 23-28 yr. Mean age of study subjects was 25.3 with SD 4.88. Women less than 33 yrs contributed to 89% of study subjects out of 64 allo-immunised women. More than half (56.25%)were 2nd gravidae. Frequency of alloimmunised women in 3rd, 4th, 5th gravidae was less.

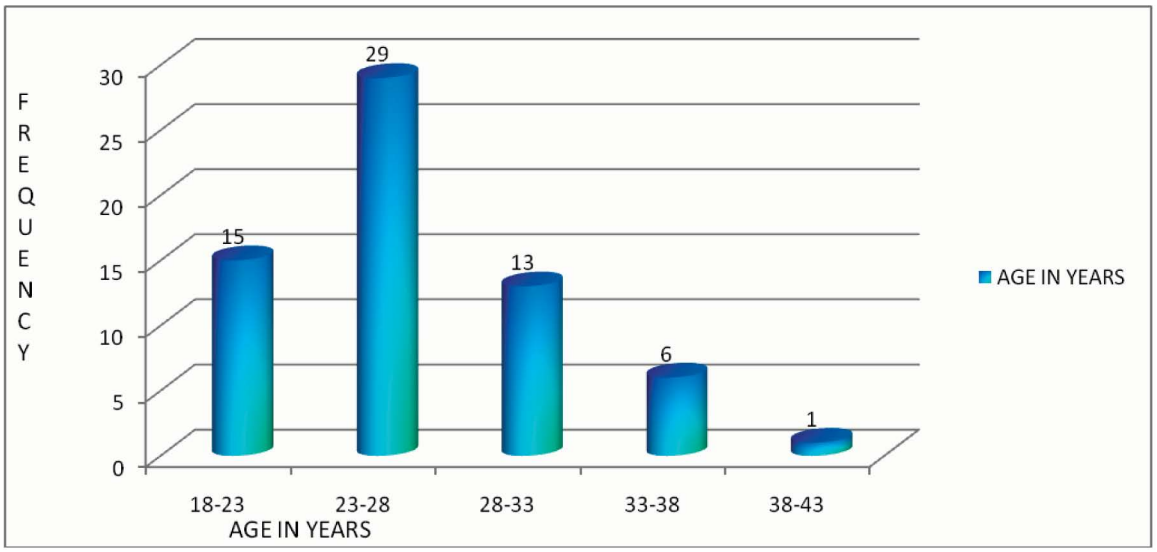

Figure 1 a. **Showing age of affected pregnancy**

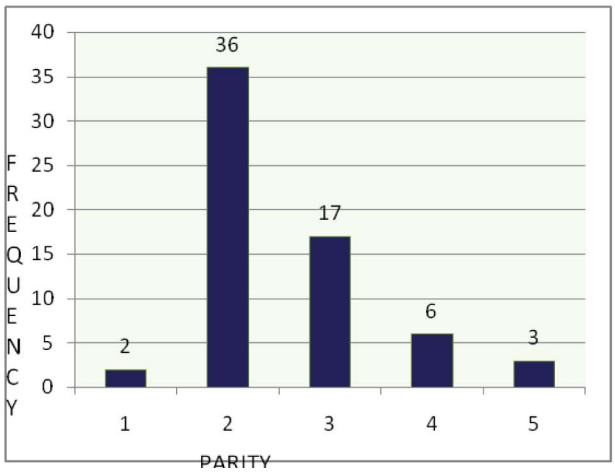

Figure 1 b. **Showing parity of affected pregnancy**

Table 1. Showing order of affected pregnancy

Affected Pregnancy	Number	Percentage
1st	46	71.87
2nd	12	18.75
3rd	3	4.69
4th	3	4.69

Of the 2 cases of alloimmunisation in primi which contributed to 3.13% of total alloimmunisations, one had history of antepartum bleeding and other did not have a relevant history. 71.8% of cases presented in the first affected pregnancy. 3rd and 4th affected pregnancies are found much less, ie 4.68% each in our study.

History of passive immunisation with Rh Ig

Failure to administer Rh Ig lead to alloimmunisation in 42 (65.6%)cases. In 14 (21.9%) cases, although Rh Ig was administered post partum, alloimmunisation occurred.8 cases(12.5%) were not able to recollect previous history of immunisation with RhIg. No study subjects received antepartum RhIg.

Mode of delivery

Vaginal (spontaneous and induced combined) constituted 62.5% of total deliveries. 62.5% cases completed term and 3 1.25% were delivered preterm. Rest 6.25% died in utero.56.25% showed adequate birth weight for gestational age (AGA). Evidence of Intrauterine growth retardation was present in 37.5%. Mean gestational age at delivery in our study was 251 days + SD 18.431.

Frequency of Hemolytic Disease of newborn

Newborns who were Rh D positive and DCT positive,

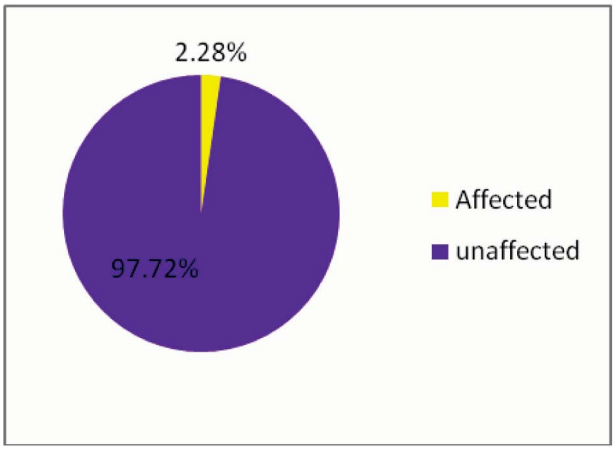

Figure 2 a. **Frequency of HDFN among Rh D negative antenatal women.**

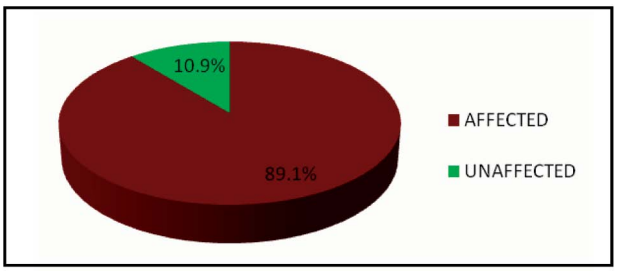

Figure 2 b. **Frequency of HDFN among alloimmunised Rh D negative antenatal women**

born to Rh D alloimmunised mothers ,were taken as affected with Hemolytic disease. Stillborn with clinical evidence of hydrops were also taken as affected.

Frequency of Haemolytic Disease of Fetus and Newborn was 57 out of 64 cases. Which constituted 2.28% of all Rh D negative females screened with ICT and 89.1% of study subjects.4 Newborns were DCT negative although Rh D positive and 3 Newborns were Rh D negative .

Rh D status of newborn

Figure 2 a & b describes the outcome of 64 Rh D alloimmunised pregnancies in terms of Rh D status and Direct Coombs Test for IgG coated red cells.

57 cases were Rh D positive and 3 were Rh D negative. In 4 cases that died in utero, Rh D status was not assessed.53 out of 57 Rh D positive newborns were DCT positive and remaining 4 were DCT negative. DCT positive infants were classified as affected and DCT negative as unaffected. Of total alloimmunised pregnancies 82.82% turned out to be DCT positive. A male preponderance was observed with male: female ratio 1.46:1.59% were males and the rest female babies)

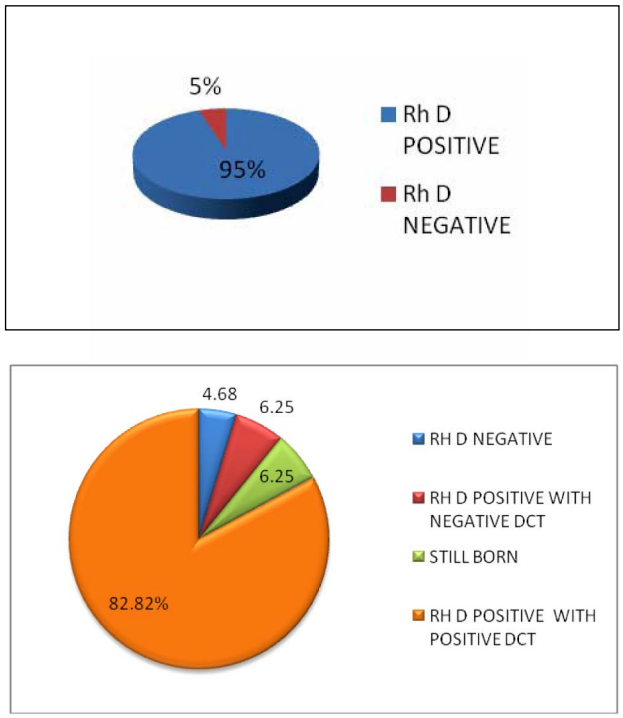

Figure 3 a & b. **Describes the outcome of 64Rh D alloimmunised pregnancies in terms of Rh D status and Direct Coombs Test for IgG coated red cells.**

DISCUSSION

The frequency of anti D antibodies detected in our study is 3.125% of all Rh D negative women. According to Global statistics HDFN prevails 0. 2% in centres with routine antenatal Rh Ig prophylaxis and 1-2% in centres with only postpartum prophylaxis[1] yet there are studies from developing countries which reported higher prevalence.[2,3,4] Slightly higher prevalence in our study may be due to a number of reasons like Referred Rh D negative cases from peripheral centres for better antenatal and neonatal care, Restricted access to health care system and post partum immunisation in some areas and absence of routine antepartum prophylaxis.

The fact that majority of cases were alloimmunised because of lack of Rh D prophylaxis in previous pregnancy shows that increasing the access and awareness to postpartum immunisation can further reduce the rate of alloimmunisation. Rh D alloimmunisation doesn't seem to increase the chances of premature delivery or caesarean section according to this study.

Majority of the off springs of alloimmunised mothers were positive for DCT for coated antibodies as consistent with many studies.[5,6] The common finding that the fetus which initiates Rh D alloimmunisation is often male is also supported in this study.[7,8]

The main limitation of this study is the limited sample size which was inadequate to find out the critical titre above which chance of moderate to severe HDFN increases. Also a community based study would have estimated the actual prevalence of the disease better. The rarity of Rh D alloimmunisation implies that multicentre long term follow up studies should be conducted to estimate the actual burden of the disease.

CONCLUSION

- The frequency of Rh D alloimmunisation observed in Rh D negative antenatal cases attending Govt. Medical College Hospital Trivandrum is 3.12% of Rh D negative women
- Failure to administer Rh Ig lead to alloimmunisation is the major cause of alloimmunisation.
- A major portion of off springs of alloimmunised mothers are Rh D positive and affected with HDFN.

END NOTE

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Conflict of Interest: None declared

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