IMPROVED PERINATAL OUTCOME IN RHESUS IMMUNISED CASES WITHOUT THE HELP OF INTRAUTERINE TRANSFUSION

by

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Introduction

From 1941 when Levine *et al* (1941) postulated the theory of isoimmunisation in Rhesus (Rh) negative mothers till 1964 when Freda (1964) started the first intrauterine transfusion (IUT), a tremendous change has taken place as regards the treatment of infants of immunised mothers. As a result, the perinatal mortality in advanced countries has been reduced to 1.5 per cent (Bowman, 1978). On the other hand, in developing countries, routine blood grouping facilities are not available in all places and Rh typing is not done as a routine even where preliminary blood bank facilities are available. The iatrogenic Rh immunisation is not a thing of past at such places.

In Postgraduate Institute of Medical Education and Research, Chandigarh, India, in the antenatal clinic, blood grouping and Rh typing is carried out as a routine. Subsequently, all Rh negative antenatal cases are managed in a special Rh clinic which is held once in a week. Since blood bank as well as good neonatology services are available in the Institute, Rh negative cases from surrounding areas are referred to this clinic. Amniotic fluid analysis by spectrophotometry to decide about the severity of disease and the timing of termination of pregnancy is used frequently and thus the mortality in the clinic due to Rh problem has been reduced to 10 per cent in booked cases.

This study presents the data regarding 100 Rh immunised cases collected over a period of 9 years (July 1970 to August 1979).

Material and Methods

Subjects included in the study were Rh negative cases identified in antenatal clinic in this hospital and cases referred by general practitioners and Government dispensaries. They were screened for Rh antibodies by indirect Coombs test (Coombs *et al* 1945) and Papain enzyme test (Goldsmith, 1955). Simultaneously husband's blood grouping, Rh typing and genotyping was also carried out as a routine.

The non-immunised cases were followed up regularly and antibody titres were repeated at 28, 32, 36 and 38 weeks of gestation. Any accompanying complication was treated accordingly. The immunised cases were seen at regular intervals and the antibody titres were re-

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peated every 2 weeks till 30 weeks and then weekly till the termination of pregnancy. If the anntibody titre was 1: 16 or higher or if there was a previous history of foetal loss or neonatal jaundice, amniocentesis was performed at 30 weeks. Placental localisation was carried out as a routine before amniocentesis (Singh *et al* 1980) and liquor amnii was subjected to spectrophotometric analysis (Liley, 1961), chemical estimation of bilirubin and other tests for foetal maturity like Lecithin/ Sphingomyelin ratio (Rodrigues *et al* 1979) and creatinine estimation (Pitkin and Zwirek, 1967). Depending on the report of spectrophotometric analysis, amniocentesis was repeated after 10 days to 2 weeks. These patients were put on Vitamin C, folic acid and other supplements as a routine. In addition phenobarbitone 60 mg three times a day for at least 2 weeks, before induction of labour was administered to all immunised cases to enhance glucoronyl transferase activity (Yeung *et al*, 1971). Labour was induced at the optimum period of gestation according to the predicted condition of foetus in utero. If labour was to be induced before 37 weeks of gestation, corticosteroid injections, 2 doses at 12 hours interval were given at least 24 hours before induction of labour to enhance the lung maturity (Liggins and Howie, 1972).

Results

During this period of 9 years, since the inception of Rh clinic, 16,524 deliveries took place in this hospital. Out of these, 1146 women were Rh negative and amongst them 100 women were immunised giving an incidence of Rh negative population in the hospital as 7 per cent and incidence of immunisation as 11.5 per cent. Out of these 100 cases, 78 were booked and 22 were unbooked. Tables I, II and III show the distribution of these

TABLE I

Distribution of 100 Cases Accordng to Gravidity in Booked and Unbooked Cases

Gravidity	Booked	Unbooked	Total
Gravida I	6	0	6
Gravida II	20	4	24
Gravida III	23	6	29
Gravida IV+	29	12	41
Total	78	22	100

TABLE II

Distribution According to Antibody Titres

Antibody titres	Booked	Unbooked
1: 1-1: 16	27	6
1: 32-1: 128	31	8
1: 256-1: 512	19	8
1: 1024 and above	1	—
Total	78	22

TABLE III

Outcome of Pregnancy and Antibody Titres

Antibody titres	Booked			Unbooked		
	L.B.		S.B.	L.B.		S.B.
1 : 1 - 1 : 16	28	(2)	—	6		—
1 : 32 - 1 : 128	30	(2)	1	8	(1)	—
1 : 256 - 1 : 512	19	(5)	2	8	(4)	3
1 : 1024 +	1		—	—		—
Total	78	(9)	3	19	(5)	3

NOTE: Figures in parenthesis are for babies born alive but lost in immediate neonatal period.
L.B.—Live born.
S.B.—Still born.

100 cases according to gravidity, antibody titres and outcome of pregnancy in booked and unbooked cases.

Amongst these 100 women, 15 had become immunised as a result of mismatched transfusion. Sixteen babies were born to them as there was one set of twins. Two of these babies were lost, one as a result of hydrops and another because of multiple congenital malformations. The corrected perinatal mortality in this group was 6.2 per cent (Table IV).

TABLE IV

Outcome of Pregnancy and Antibody Titres in Cases With History of Mismatched Transfusion

Antibody titres	Live born	Still born
1 : 1 - 1 : 16	3	—
1 : 32 - 1 : 128	9 (1)	1
1 : 256 - 1 : 512	3 (1)	—
1 : 1024 +	—	—
Total	15 (2)	1

NOTE: Figures in parenthesis are for babies born alive but who died in immediate neonatal period.

Figures 1 and 2 show the graph plotted for cases No. 84 and 100 depicting the spectrophotometric analysis and optical density difference at 450 mμ respectively. These graphs were plotted by automatic BeckMan's spectrophotometer on semilog graph paper.

In all, 103 babies were born as there were 3 sets of twins. Out of these, 6 babies were still born, another 14 were lost within the first seven days of life, thus the perinatal mortality being 19.4 per cent. But if the deaths due to causes unrelated to immunisation are excluded, the corrected perinatal mortality for booked and unbooked cases is 10.1 and 28.6 per cent respectively.

Amniocentesis was performed 91 times in 71 women. The prediction was wrong

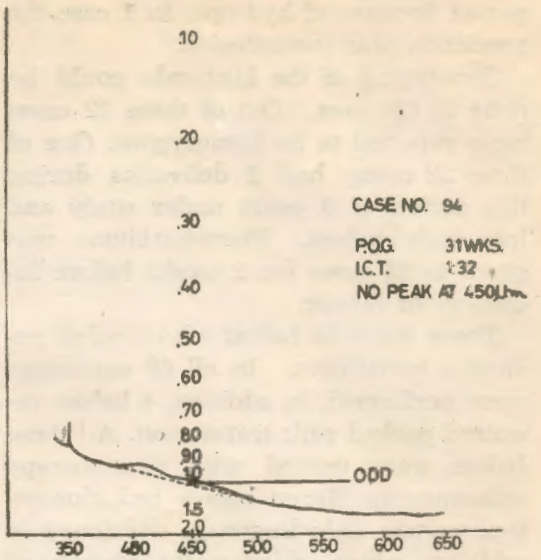

Fig. 1

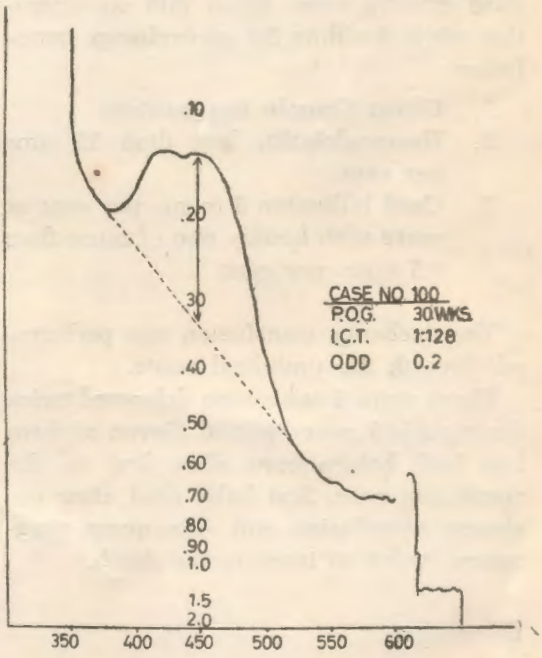

Fig. 2

in 3 cases delaying termination. Though all these 3 babies were born alive, they died in the immediate neonatal

period because of hydrops. In 1 case the prediction was inconclusive.

Genotyping of the husbands could be done in 63 cases. Out of these 22 cases were reported to be homozygous. One of these 22 cases, had 2 deliveries during this period of 9 years under study and lost both babies. Phenobarbitone was given to 75 cases for 2 weeks before induction of labour.

There were 43 babies who needed exchange transfusion. In all 68 exchanges were performed. In addition, 4 babies required packed cells transfusion. All these babies were treated with phototherapy subsequently. Seven babies had glucose-6-phosphate dehydrogenase deficiency in addition, which added to the severity of hyperbilirubinaemia. The following standard criteria were taken into consideration while deciding for an exchange transfusion:

1. Direct Coombs test positive.
2. Haemoglobulin less than 12 gms per cent.
3. Cord billirubin 6 mgms per cent or more with hourly rise of more than 0.5 mgm per cent.

The exchange transfusion was performed through the umbilical route.

There were 8 cases who delivered twice during this 9 years' period. Seven of them had both babies born alive but in the remaining case, first baby died after exchange transfusion and subsequent pregnancy ended in intrauterine death.

Discussion

With the advent of an effective means of prevention of immunisation by administration of injection Anti D (gamma globulin) post delivery as well as antenatally in selected cases and good blood bank facilities, it is thought that the problem of isoimmunisation may be eradicated in the near future in the developed countries. On the other hand, in the developing countries, it is going to take years before even the administration of Anti D post delivery becomes a routine. The present study has shown that mismatched transfusion was responsible for 15 per cent of immunised cases. The corrected perinatal mortality in these 15 cases was 6.2 per cent, whereas in a study by Krishnan *et al* (1973) only 40 per cent babies could be salvaged in those cases whose mothers had been immunised as a result of mismatched transfusion. The antibody titres were also higher in the above mentioned study, whereas in the present study, the levels are not different when compared to the whole group.

The incidence of Rh negative population in this part of the country is 3.6 per cent (Anees *et al*, 1972), whereas in the present series it was 7 per cent. The incidence of immunised cases was 11.5 per cent which is again high. Both these findings can be explained on the basis that this hospital is a referral centre and thus known Rh negative antenatal cases and immunised pregnant women are referred for management here.

The estimation of antibody levels is a screening method only, though some believe that if it is carried out by same individual using same technique and same Rh positive cells, it is of some prognostic significance. But there are so many other factors on which prognosis depends like binding constant of the Rh antibody, Rh antigen content of the foetal red cells membrane and ability of the foetus to replace destroyed red cells without compromising hepatic function (Bowman, 1978). Therefore, one should not depend on the levels of antibodies only but spec-

trophotometric analysis of the liquor amnii should be used to predict the condition of foetus in utero.

In the present series, spectrophotometric analysis was correct in all cases except 3, as a result of which all these 3 babies were lost because of delayed intervention. Such life threatening spectrophotometric inaccuracies are known which could result in too early or too late intervention in 2-3 per cent of Rh isoimmunised pregnancies (Bowman, 1978).

Out of 6 primigravidae, there was only 1 who had a history of mismatched transfusion. In the rest 5 cases, no history of previous abortion or transfusion could be obtained. The immunised status of these 5 women could perhaps be explained on the basis of the passage of Rh positive maternal red cells at the time of their birth (Taylor. 1967), the grand mother theory giving rise to antibody in the early neonatal period. and Rh positive baby in utero acting as a second stimulus. Unfortunately, the blood grouping and Rh typing of the mothers of these 5 primigravidae could not be done.

The overall perinatal mortality was 19.4 per cent but if the perinatal deaths due to causes unrelated to immunisation are excluded, the corrected perinatal mortality was 10.1 and 28.6 per cent in booked and unbooked cases respectively. In the recent series the perinatal mortality in the Rh isoimmunised cases had been reduced further with the use of a IUT in cases where development of hydrops is expected before 32 weeks of gestation. Attempts at IUT were made in this Institute but were unsuccessful. Comparing the perinatal mortality in unbooked cases, it is thought that since the primary mortality of the procedure like IUT is reported to be 10 per cent even in well established centres nothing has been lost in the present set up by this facility not being available. Though Bowman (1978) has been able to reduce the perinatal mortality of 1.5 per cent which is an isolated report, generally accepted perinatal mortality rate from erythroblastosis in other parts of Canada and other developed countries at present is in the order of 5-10 per cent, to which the perinatal mortality in booked cases in our data compares very well.

Conclusion

Data regarding the improved perinatal mortality in 100 Rh immunised cases is being presented. These cases were managed in the Rh clinic in the department of Obstetrics and Gynaecology, Postgraduate Institute of Medical Education and Research, Chandigarh. Though the perinatal mortality in developed countries has been reduced to 1.5 per cent with the aid of intrauterine transfusion and recent advances like plasmapheresis, in places where such facilities are not available perinatal mortality is still high. In the present series with the help of regular antenatal care, spectrophotometric analysis and timing the delivery at optimum period of gestation, the perinatal mortality in booked cases has been reduced to 10.1 per cent which compared well with the figures in any good centre in developed countries.

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