RH FACTOR IN OBSTETRICS

By

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An Obstetrician is mainly concerned with Rh factor, while dealing with a Rh negative parturient harbouring a Rh positive foetus. The essence of the problem in such cases is that foetal erythrocytes carrying antigen from Rh positive foetus cross the foeto-maternal barrier and enter the maternal circulation resulting in antibody formation. These antibodies affect that foetus adversely. In order to find out the incidence of Rh factor and foetal outcome in Rh negative mothers attending antenatal clinic of Lady Hardinge Hospital, this study was undertaken in the Dept. of Obstetrics and Gynaecology. It included 3270 cases who were screened for ABO and Rh grouping. Out of these 3070 were with history of abortion, stillbirth or neonatal death. Two hundred cases were selected at random as a control study.

Observations and Discussion

Incidence of Rh-Factor

Since the Rh factor is genetically transmitted, there is variation in the incidence of Rh negative population in different communities. Incidence of Rh negative population in white races varies from 15% (Landsteiner and Weiner, 1940) to 17% (Mollison and Cutbush, 1949).

Indian workers from various parts of India have reported incidence varying from 2.7-10% (Table I). Our incidence of 8.6% is comparable with the incidence of Rangnathan *et al* from Madras (1948) and Talwar and Sawhney (1959) from Punjab.

It is evident from this Table that incidence of Rh negative factor is lower in the Eastern and Western parts of the

TABLE I

Comparison of Rh Negative Incidence From Various Parts of India

Year	Author	Nature of Population	Total No. of cases	Percentage of Rh. Neg.
1944	Das Gupta	Calcutta	240	10
1948	Ranganathan	Madras	294	8.50
1959	Roy	Bengal	1,435	5.29
1959	Talwar	Punjab	1,000	7.3
1962	Anand	Rajasthan	1,000	2.70
1963	Radav	Kanpur	1,680	3.39
1964	Sheth & Purandare	Bombay	27,560	3.66
1967	Usha Krishna	Bombay	24,289	4.60
1971	Present Series	Delhi	3,270	8.6

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country. We are unable to offer any explannation for this difference.

In Western countries, the difference in Rh negative incidence in the general population (15%) and in the mothers with obstetrical mishap (12.4%) reported by Morrison and Meacock (1945) was not significant. Similarly, no statistically significant difference was found in the two groups studied by us. The incidence of Rh negative was 8.6% in study group, and 8% in control group. (P was between .7 to .75). Therefore, it seems imperative that all expectant mothers should be screened for Rh factor and this investigation should not be limited only to the mothers with the history of obstetrical mishap.

No difference of Rh distribution in relation to ABO blood group was observed which is in accordance with that of Sheth and Purandare (1964) and Krishna (1966).

Incidence of Immunization

Though statistically there are 12% marriages involving mating of Rh positive husband with Rh negative wife (Hunt, 1947) the incidence of immunization reported is only 1.40 to 6.40% (Table II).

TABLE II

Incidence of Isoimmunization

S. No.	Author	Year	Incidence of immunization
1.	Donohue	1954	5.60
2.	Potter	1958	5.00
3.	McElin	1962	6.40
4.	Sheth & Purandare	1964	6.20
5.	Eastman, N. J.	1966	4.72
6.	Usha Krishna	1967	5.70
7.	Trivedi, D. M.	1968	1.40
8.	Present series	1971	12.5

This is due to the fact that sensitization depends upon the zygosity of husband, transfer of antigen across the foeto-maternal barrier, response of host to form antibodies, and ABO incompatibility of the couple. We observed an incidence of immunized mothers to be 12.5% in the study group. This incidence is higher than the figures quoted by other authors. It could be due to the selective nature of the study.

Age and Parity

Present study revealed that in the age group of 21-30 years, 10.30% of Rh negative mothers were immunized as compared to 15.40% in the age group of 31-40 years. It was also noted that 70% of the immunized mothers were between para 2 to 5, highest incidence being in para 5.

Sheth and Purandare (1964) reported that in immunized group maximum patients were of second parity. Trivedi (1968) observed that 55% of the total cases were between para 2 to 4 and 20% were para 5 and above. It is logical to expect that during each pregnancy and confinement, the mother is exposed to risk of immunization and, therefore, greater number of women would be immunized as the parity increases. Since there is correlation between advancing maternal age and parity, chances of immunization increase with the advancing age. We did not observe any of the primigravidae with Rh antibodies. Involved infant during first pregnancy usually indicates previous blood transfusion with Rh positive blood. However, Bhatia and Sanghvi (1959) found antibodies in a primigravida without previous history of blood transfusion. Pregnancy induced immunization in first pregnancy rarely results in erythroblastotic infant.

Previous Obstetrics History in Relation to the Maternal Sensitization and Foetal Outcome

Relationship between previous obstetric history and prognosis of newborn with Rh iso-immunized mothers is rather complicated. Levine *et al,* (1941) reported that there was higher incidence of repeated abortions, stillbirths and neonatal deaths in sensitized mothers. The cases studied by us showed that the incidence of stillbirths was 23.07% in immunized mothers and 10.65% in non-immunized mothers. The figures for neonatal deaths were 30.77% and 16.88%, respectively. This was found to be statistically significant ($P < .05$). Walker and Murray (1956) pointed out that it is important to know whether abortion had occurred before or after the immunization. They reported 17% stillbirths in the former group and 46% stillbirths rate if abortion occurred following immunization.

Diamond (1950) stressed increased severity of disease in later babies because of statistically significant increase in stillbirths, neonatal deaths and decrease in mild form of disease. Many authors have concurred with this view either by showing better prospects for first affected child, (Allen *et al,* 1950; Mollison and Cutbush, 1954) or worse prognosis in later babies (Potter, 1948; Nevanlinna, 1953; Zuelzer, 1948; Allot, 1951; and Walker and Murray, 1956).

If previous infant was clinically unaffected but had weakly positive Coomb's test the survival rate was 95% (Jacob 1959). In case previous baby was mildly affected, the survival rate was 60% without treatment and 40% required exchange transfusion (Walker and Murray, 1956). In this group Goplerud (1961) reported 74% survival rate. Jacobs (1959) reported 68.7% survival rate among mothers having had delivered mild to moderately severe erythroblastotic infants who survived following treatment and if mother had delivered erythroblastotic infants not surviving neonatal period, all the newborns were either stillbirths or died during neonatal period. Goplerud (1961) reported 45% survival rate in this group, whereas Potter (1958) noted it to be 10-20%. Among patients with previous history of one or more hydropic stillbirths, Potter (1958) reported 10% survival, Goplerud (1961) noted 26%, whereas in the series of Jacobs (1959) all the newborns were stillborn.

Maternal Antibody Titre and Foetal Outcome

Relationship between antibody titre and foetal outcome is a subject of controversy. Walker and Mollison (1957) reported lowest antibody titre at which hemolytic disease appeared was 1:32 whereas Sheth (1964) observed it to be 1:16. Krishna (1966) noted most of normal infants with the titre less than 1:16 and stated that with the titre of 1:64 all the neonates were affected who required exchange transfusion.

We observed good correlation between maternal antibody titre and foetal outcome (Table III). The antibody titre at which haemolytic disease appeared was 1:8 and the number of stillbirths and erythroblastotic infants increased with the higher titre. Exchange transfusion was given to 11 infants of which 7 survived.

We found rising antibody titre in 17% cases. Frisch (1949) found rising titre in 61:89% whereas, Walker (1957) reported rising titre in 41 of his cases. Freda (1962) claimed that antibody titre was of limited value in judging the prognosis of foetal outcome since the titre remained at constant level among 80% of her cases

TABLE III

Relationship of Maternal Antibody Titre to Foetal Outcome

Maternal antibody titre	No. of cases	Late abortion	Still-birth	Jaundice	Exchange trans-fusion	Survival
1:4	1	—	—	—	—	1
1:8	1	—	—	1	1	1
1:16	5	—	—	5	4	2
1:32	5	—	1	4	3	2
1:64	8	—	3	5	3	1
1:128	5	—	5	—	—	—
1:256	3	2	1	—	—	—
Total	28	2	10	15	11	7

inspite of varying foetal outcome.

Table IV shows behaviour of antibody titre and foetal outcome among Rh immunized cases with rising titre. Out of 5 infants born in this group only one survived, thus giving 20% survival rate, while in the group of cases with constant titre survival rate was 30%.

It has been pointed out that the time period for which foetus is exposed in utero to certain amount of antibodies has great significance (Page *et al*, 1946; Murray and Taylor, 1949). Kelsall (1958) used the term titre-time index and demonstrated that with the titre of 1:64 at 32nd weeks of gestation all foetuses were affected, either they died or were given exchange transfusion, whereas 72% of the infants at the same period of gestation with 1:32 titre required exchange transfusion.

McElin (1962) observed 14.6% survival rate when antibodies were already present at 20th week of gestation as compared to 85.7% with the appearance of antibodies at 24 weeks. Higher titre starting from the earlier period of pregnancy affects the foetus adversely.

In our study no antibodies were detected in non-immunized Rh negative mothers and no change in titre was noticed in immunized cases, 10 days to 2 months following delivery. It would be interesting to have follow up of patients for longer period to find out the time of appearance of antibodies and whether there would be any change in titre in the immunized cases.

TABLE IV

Behaviour of Antibody Titre and Foetal Outcome Among Rh. Immunized Cases With Increasing Titre

Case No.	Period of gestation in weeks						Foetal outcome
	20	20-23	24-27	28-31	32-35	36-40	
99	Nil	Nil	Nil	1:32	1:32	1:64	Hydrops foetalis died
108	—	—	—	—	—	1:32	Exchange Transfusion Survived
175	Nil	1.256	1:256	1:256	—	—	Still Birth
181	Nil	1:128	1:128	1:128	—	—	Still Birth
195	Nil	Nil	1:64	1:64	1:64	—	Exchange Transfusion; Died

Relationship of Cord Blood Bilirubin to Erythroblastosis

We observed good correlation between cord blood bilirubin and affliction of foetus with erythroblastosis (Table .V).

TABLE V

Showing the Serum Billirubin Levels of Blood Samples From Umbilical Cord in Normal and Affected Infants

Serum Bilirubin level	Infants with mild jaundice	Infants with severe Jaundice	Normal
0-2.99 m.gms%	5	—	14
3-5.99 m.gms%	—	5	1
6-⩾6 m.gms%	—	1	—

Of the term infants who developed jaundice during neonatal period, 5 had jaundice of mild degree and their cord bilirubin at birth was 3 mgm%. Five infants with cord bilirubin of more than 3 mgm% developed severe jaundice, of which 4 were given exchange transfusion. Similar findings were observed by Allen and Diamond (1950). In their series, 93% of normal infants had cord bilirubin less than 3 mgm%, whereas 79% of infants with erythroblastosis had bilirubin more than 3 mgm%. Sheth (1964) reported cord bilirubin less than 5 mgm% in 404 infants out of which 5 required exchange transfusion, while out of nine babies with cord blood bilirubin more than 5 mgm%, 5 needed exchange transfusion. Trivedi (1968) reported that in her series five infants who required exchange transfusion had cord bilirubin more than 3 mgm%. Therefore, it may be concluded that a newborn with cord bilirubin of 3 mgm% or above should be kept under constant observation in order to give proper treatment in time.

Summary

1. 3070 cases with bad obstetric history attending the antenatal clinic at Lady Hardinge Hospital were screened for ABO & Rh grouping. Two hundred cases were selected at random as a control study. In the study group incidence of Rh negative was 8.6% and in control group 8%.

2. Incidence of immunization in the study group was 12.5%.

3. 70% of the immunized mothers were between para 2 to 5, highest being in para 5.

4. In age group of 21-30 years, 10.30% of the mothers were immunized as compared to 15.40% in the age group of 31-40 years.

5. Incidence of stillbirths and neonatal deaths among immunized mothers was 23.07% and 30.77%, respectively as compared to 10.65% and 16.88% among non-immunized mothers.

6. Antibody titre at which haemolytic disease appeared was 1:8. With the higher antibody titre, number of stillbirths or neonatal deaths also increased. Increase in antibody titre was noted in 17% of immunized cases.

7. Infants born with cord blood bilirubin of more than 3 mgm% developed haemolytic disease and most of which required exchange transfusion.

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