ROLE OF RUBELLA VIRUS IN CASES OF ABORTIONS

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Introduction

The role of the rubella virus in the causation of foetal wastage by way of congenital defects, abortions and premature deliveries is well documented in Western literature (Sever *et al.*, 1969; Dudgeon *et al.*, 1967). There is however, an impression amongst Indian workers that this factor does not operate here. In an attempt to question this outlook, a few studies have been carried out in Delhi (Seth *et al.*, 1971), Lucknow (Mathur *et al.*, 1972, Chaturvedi *et al.*, 1976) and Calcutta (Chakraborty *et al.*, 1973). This study has been an extension of the previous work in Lucknow and was performed in order to assess the exact magnitude of the problem prevailing amongst obstetric patients.

Material and Methods

Cases: The cases undertaken for this study comprised of patients attending outpatient clinics or admitted to the wards of the Department of Obstetrics and Gynaecology, K.G.'s Medical College, Lucknow. They included patients attending the routine antenatal clinics at various periods of gestation and cases of threatened, inevitable and incomplete abortions.

Haemagglutination inhibition test: Sera from these cases were studied for the presence of haemagglutination inhibition (HI) antibodies using the micro-technique of Halonen *et al* (1967). Doubling dilutions of the sera were used starting from 1:10. The freeze dried rubella haemagglutinin antigen was kindly supplied by Dr. M. S. Pereira, Virus Reference Laboratory, Colindale, London. The details of the technique have been described earlier (Mathur *et al.*, 1974).

The IgM antibodies were estimated by the technique of Banatvala *et al* (1967). The sera were treated with 2-mercaptoethanol (2-ME). A four fold decrease in the titre shows the presence of IgM antibodies.

Results

The present study was undertaken to find out the significance of rubella antibodies in cases of abortions. A total of 190 cases of abortions were studied. In some of them multiple samples of blood were collected at regular intervals.

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Ninety cases of normal healthy controls of matching age groups were taken.

The distribution of HI antibodies in different age groups in cases of abortion and control has been shown in Table I. In the age group 15 to 20 years, out of 28 patients 15 (53.5 per cent) had rubella antibodies. With the increasing age, the incidence of antibodies increased reaching a peak 84.6 per cent at the age of 26 to 30 years, then declined to 55.5 per cent in the age group above 35 years. Not much difference of per cent positivity of HI antibodies was seen compared to controls.

Out of a total of 190 cases of abortions, 75 were of threatened abortion and 115 were of incomplete or inevitable abortion. An attempt was made to find out any correlation, if present, in the incidence and titre of HI antibodies between the two groups of abortion and control. Among the cases of threatened abortion, the antibodies were present in 41.6 per cent of cases in 15-20 years age group. There was gradual increase with the age and in age group above 35 years, 80 per cent of cases had antibodies. The overall incidence of antibodies was 68 per cent while in control it was seen in 70 per cent of cases (Table II). Out of 115 cases of incomplete and inevitable abortion HI antibodies were seen in 75 (65.2 per cent cases. Not much difference in per cent positivity in different age groups was observed except above 35 years. In this group, antibodies were present in 55.5 per cent of cases while in the same age

TABLE I

Incidence of Rubella Antibodies in Cases of Abortions and Controls

Age group	Abortion Patients			Controls		
	Total No. of cases	Number positive	Per cent Positive	Total No. of cases	Number Positive	Per cent positive
15-20	28	15	53.5	18	10	55.5
21-25	65	44	67.6	23	16	6.9
26-30	75	55	68.0	25	17	68.5
31-35	13	11	84.6	16	14	87
35	9	5	55.5	8	6	75
Total	190	126	66.6	90	63	70

TABLE II

Incidence of Rubella in Cases of Abortions

Age group	Threatened abortions		Incomplete and inevitable abortion	
	Total No. of cases	Positive cases	Total No. of cases	Positive cases
15-20	12	5 (41.67)	16	10 (62.5)
21-25	33	24 (72.73)	32	20 (62.5)
26-30	25	18 (72)	50	33 (66.0)
31-35	5	4 (80.0)	8	6 (75.0)
35	—	—	9	5 (55.56)
TOTAL	75	51 (68%)	115	75 (65.22%)

group in controls it was recorded in 75 per cent of cases (Table III).

An analysis of antibody titres both in cases of abortion and control showed some interesting findings which are presented in Table III. Out of 75 cases of threatened abortion, 51 had titre of 20 or more. Only in 1 case, titre of 320 was observed. The mean HI titre of this group was 55.2. High titres were recorded in cases of inevitable or incomplete abortion. Out of 115 cases, 75 had titre above 20. Out of this, 2 cases had titre of 320 and 2 of 640. The mean HI titre in the two group of abortions is quite marked. Among the control group 63 out of 90 cases had titre 20 or above. Only 1 had titre of 320. The mean HI titre was only 51.5 (Table III).

TABLE III

Rubella Antibody Titre in Cases of Abortions and Control

Cases	Total No.	Antibody titre							Mean HI titre
		10	20	40	80	160	320	640	
Threatened abortion	75	24	23	13	9	5	1	-	55.2
Incomplete or inevitable abortion	115	40	29	24	12	6	2	2	68.5
Control	90	27	33	15	8	6	1	-	51.5

The cases of abortion showed definite reduction in HI titre after treatment of sera with 2-ME (Table IV), indicative of recent infection with rubella virus. Blood from these 10 cases was collected at the time of abortion. Four aborted later and only 1 patient had a normal live baby born at term. The serum of this patient was collected in the second trimester and hence it is probable that the foetus escaped during the period of organogenesis when it is most liable to develop congenital malformation. Of those who aborted later, 2 had serial samples taken and both showed an increase of HI and IgM titres which can conclusively prove that the cause of the abortion was rubella virus. It is noteworthy that even those patients who showed an increase in titre in successive samples indicative of infection in the intervening period, there was no history clinically suggestive of rubella infection hence it must have been a subclinical infection. Thus of an initial total of 190 abortion patients, in 9 patients rubella could be incriminated as the causative agent giving an incidence of 4.74 per cent which is fairly high.

TABLE IV

Abortion Cases With Significant IgM Titres

Sl. No.	Type of abortion	RUBELLA ANTIBODIES	
		HI Titre	IgM
1.	Threatened abortion	160	40
2.	Incomplete abortion	320	80
3.	Incomplete abortion	40	10
4.	Incomplete abortion	640	160
5.	Threatened abortion	160	40
6.	Incomplete abortion	640	160
7.	Incomplete abortion	320	80
8.	Theatened abortion	40	10
9.	Threatened abortion	80	20
10.	Threatened abortion	80	20

Discussion

In the present study, the HI antibodies

against rubella virus were seen to be present in 70 per cent in normal pregnant females and 66.6% in cases of abortions. The antibodies increased with increasing age. The maximum incidence of 87% sero-positivity was observed in the age group of 31-35 years. High incidence of HI antibodies have been reported from other countries also e.g. 90% in Spain (Najera *et al.*, 1973), 95% in Taiwan (Gale *et al.*, 1969) and 80% in Carribbean (Dowdle *et al.*, 1970). Our findings are similar to Mathur *et al* (1974) who had shown previouslly that 15-20% women of child bearing age in Lucknow do not have rubella antibodies. In India, Seth *et al.*, (1971) have reported the incidence in Delhi where it varies from 77.5 to 88% in different age groups while in Calcutta a low incidence of 53.14% was reported by Chakraborty *et al.*, (1973). Amongst pregnant females higher incidence or rubella antibodies have been reported from many Western countries e.g. 95% from Manchester (Manson, 1960), 93% from Helsinki (Vesikari *et al.*, 1968), 91% from U.S.A. (Sever *et al.*, 1968) and 87% from Stockholm (Svedmyr *et al.*, 1967). A lower incidence of antibodies has been reported from Jamaica, Trinidad (Pitts *et al.*, 1969), Hawaii (Sever *et al.*, 1969), Japan Kono, 1969) and Thailand where the highest proportion of immune-response varies from 67% to as law as 42% in Hawaii (Sever *et al.*, 1965). Latitude differences as a possible cause is not probable as suggested by Sever *et al.*, (1969). Racial insusceptibility and ethnic differences have been ruled out by Rawls *et al.*, (1967) but Kono from Japan (1969) postulates that the difference in susceptibility may be due to the different biological properties amongst the Japanese poplation as well as the Japanese strains of rubella virus.

In this study, levels of HI antibodies and IgM were estimated in the sera. The importance of IgM antibodies lies in the fact that its presence denotes recent infection, whereas the presence of HI antibodies in the serum is indicative of immunity acquired at some time in the past.

The findings of the mean HI antibody titres in patients of threatened abortion, incomplete or inevitable abortions and controls were analysed. It was observed that mean HI titre was significantly high in cases of incomplete or inevitable abortion while not much of difference was observed between the cases of threatened abortions and control (Table II). Thus, our findings indicate role of rubella virus in cases of incomplete or inevitable abortions.

The role of rubella virus in the etiology of abortions was confirmed in 10 patients by demonstration of IgM antibodies. Of these 10 patients, 5 were of incomplete abortion and 5 were of threatened abortion. Out of 5 patients of threatened abortion, 4 later aborted and 1 had a normal healthy child delivered at term. Of the 4 patients that aborted, from 2 repeated blood samples were collected at 7 to 10 days intervals. A gradual increase in HI titre and IgM antibodies were demonstrated in them. It can be deduced that out of 190 patients studied, in 9 patients rubella was the causative factor of abortion. This figure of 4.74% is comparable with the incidence quoted by Dudgeon *et al.*, (1967) who have reported an abortion rate of 5% for women infected with rubella in the first 12 weeks of pregnancy and 0.8% in those women acquiring the infection after the 13th week while in controls it was 2.4% and 0.05% respectively. It was difficult to diagnose cases of rubella as patients did not give history or showed signs suggestive of rubella infection. Hence, we would like to point out that the diagnosis of rubella is not pos-

sible on clinical grounds only.

These data stress that the magnitude of the problem of rubella infection in India is fairly great. To eradicate the susceptibles amongst the population at risk large scale immunization of adolescent girls prior to marriage or conception should be mandatory.

Summary and Conclusion

1. The incidence of rubella positive patients in thls study was 71.67%.

2. Amongst pregnant patients, 70.92% were rubella positive.

3. Results of 190 aborted patients studied were—Threatened abortion—65% seropositive Incomplete abortion—62.22% seropositive.

4. Patients of incomplete abortion showed a higher mean level of HI antibody 68.5 than the threatened abortion patients.

5. Rubella as the causative factor could be conclusively proved in 4.74% cases of abortion.

6. A significant lack of clinical history and signs suggestive of rubella was observed despite the high incidence of rubella positive patients in the study.

7. Serial estimations of rubella antibody titre were done in some cases, rising titres are indicative of amount with rubella virus. Clinical features of rubella were conspicuously absent even in cases showing rising titres of HI antibody and IgM.

8. In view of all the above facts it is concluded that it should be made essential to test every patient in the Ist trimester of pregnancy for antibody to rubella and large scale immunization of the susceptible population should be undertaken.

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