EFFECT OF PREGNANCY ASSOCIATED HYPERTENSION ON IMMUNOGLOBULIN LEVELS IN NEWBORNS

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ABSTRACT

In a prospective study of 124 neonates born to mothers with normal pregnancy and pregnancy associated hypertension (PAH), serum IgG, IgA and IgM were estimated by single radial immunodiffusion technique. Significantly low levels of IgG were found in mothers having PAH, as compared to normal pregnancy ($p < 0.001$), whereas IgA and IgM showed no difference in the two groups. There was no statistical difference in maternal and cord blood IgG in either the control or study group. IgG was significantly higher ($p < 0.001$) in cord blood of babies born by vaginal route as compared to forceps (via vaginal route) or cesarean section. IgA and IgM levels did not vary with mode of delivery.

Key words: *Fetal immunoglobulin, Pregnancy associated hypertension, Mode of delivery.*

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Received for publication June 26, 1989; Accepted January 25, 1992

Immunological profile of cord blood of newborn babies varies with the antenatal course(1), mode of delivery(2), nutritional status of mother(3), period of gestation(4) and congenital infections(5,6). IgG is the only immunoglobulin (Ig) which crosses the placenta. Most newborns tend to have normal IgG levels, regardless of whether the maternal concentration of IgG is elevated or depressed. IgA and IgM do not cross the placenta, they are synthesized to a negligible extent in fetal life(7). Elevated levels of IgA and IgM in cord blood may be of use in diagnosing congenital infections(5,6). Altered Ig profile has been reported in mothers having pregnancy with hypertension and toxemia(8). We conducted this study to find out the effect of altered immunological profile in mothers having pregnancy associated hypertension (PAH) over the immunological profile of the cord blood of newborns.

Material and Methods

The present study was conducted at Jawaharlal Nehru Hospital, Aligarh in the Departments of Obstetrics and Gynecology, Pathology and Microbiology from January 1986 to December 1987. It comprised of 150 mothers in the age group of 18-38 years in their third trimester of pregnancy (37-40 weeks gestation). Fifty mothers with normal pregnancy served as controls, 45 had associated pre-eclampsia or eclampsia, and 55 had pregnancy with essential hypertension. Cord blood immunoglobulin profile of 124 live babies born to these mothers was studied. Forty eight babies were born to mothers with normal pregnancy and 76 to mothers with PAH.

Five ml venous blood was collected from mother in the third trimester, and 5 ml of umbilical cord blood of baby during

delivery, in dry sterilized plain vials. Serum was separated and stored at –20°C. Immunoglobulins (IgG, IgA and IgM) were estimated by Single Radial Immunodiffusion technique(9). Statistical evaluation was done by Students 't' test when sample size was less than 30, and by 'Z' test where sample size was above 30.

Results

IgG was significantly low ($p<0.001$) in mothers having pre-eclampsia and eclampsia (1276.2 ± 276.15 mg/dl) or essential hypertension(1270.1 ± 325.28 mg/dl) as compared to normal pregnancy (1621.62 ± 370.16 mg/dl), but there was no significant difference between the two subgroups of PAH (*Table I*).

Cord blood IgG levels were significantly higher ($p<0.001$) in babies born by normal vaginal delivery (1514.2 ± 225.60 mg/dl) as compared to babies in whom forceps was applied during vaginal delivery to cut short the second stage of labor (1245 mg/dl), and those born by cesarean section (1290 mg/dl). Similar observations were seen in babies born to mothers with pre-eclampsia and eclampsia or essential hypertension (*Table II*).

IgA and IgM were present in cord blood in 17 out of 48 (35.4%) babies born to mothers with normal pregnancy and 46.6 and 36.6%, respectively with pre-eclampsia and eclampsia and 41.3 and 32.6%, respectively in mothers having essential hypertension (*Table I*). Of 17 babies born to mothers with normal pregnancy, 6 gave a history of prolonged labor, 3 PROM (premature rupture of membranes) and in the rest no apparent cause of rise in IgA and IgM could be detected.

No significant correlation was found in cord blood IgG, IgA and IgM levels in babies with birth weight ranging from 2.0 to 3.5 kg in both normal pregnancy and pregnancy associated hypertension (*Table III*).

Discussion

IgG was significantly low ($p<0.001$) in mothers having pregnancy associated hypertension (PAH) as compared to normal pregnancy. Lowering of serum IgG in mothers having PAH could be accounted for by various theories *e.g.,* increased production of steroids during pregnancy(10), selective transplacental passage of maternal antibodies to fetus(2), loss of IgG in the urine due to proteinuria(11) and dilutional effect due to physiological hydremia(12).

There was no significant difference ($p>0.05$) in the levels of IgG in cord blood of newborns and mothers' serum in both normal pregnancy and PAH, thereby, suggesting that IgG level in fetus is not affected by maternal concentration of IgG. The placental transfer of IgG took place irrespective of the maternal levels of IgG which were lowered in PAH. Giltin(7) has explained this by demonstrating that the maternal-fetal placental transfer of IgG is regulated by two mechanisms. The first is a passive transfer of maternal IgG across the placenta, which increases with gestational age. The second is an enzymatic mechanism for the active transport of maternal IgG to the fetus.

We observed elevated IgG levels in fetus born by normal vaginal route as compared to cesarean section or in whom forceps was applied during vaginal delivery to cut short the second stage of labor. A similar trend was observed by others(13,14). Jones and Payne(2) have also suggested that uterine contractions are associated with marked pressure changes

TABLE I—*Serum IgS Concentrations in Maternal and Cord Blood in Normal Pregnancy and Pregnancy Associated Hypertension*

Group	IgG (mg/dl)		IgA (mg/dl)		IgM (mg/dl)	
	Maternal serum	Cord blood	Maternal serum	Cord blood	Maternal serum	Cord blood
1. Normal pregnancy	1621.62 ± 370.16 (n = 50)	1489.55 ± 358.3 (n = 48)	215.39 ± 63.03 (n = 50)	48.51 ± 66.87 (n = 17)	211.51 ± 46.47 (n = 50)	47.74 ± 17.65 (n = 17)
2. Pregnancy with pre-eclampsia and eclampsia	1276.2 ± 276.15 (n = 45)	1314.33 ± 232.2 (n = 30)	204.39 ± 56.42 (n = 45)	57.4 ± 65.12 (n = 14)	215.67 ± 83.34 (n = 45)	89.08 ± 62.6 (n = 11)
3. Pregnancy with essential hypertension	1270.1 ± 325.28 (n = 55)	1305.4 ± 251.3 (n = 46)	187.0 ± 81.68 (n = 55)	34.9 ± 4.66 (n = 19)	195.94 ± 48.91 (n = 55)	63.9 ± 24.18 (n = 15)
p value 1 : 2	<0.001	<0.01	NS	NS	NS	<0.01
1 : 3	<0.001	<0.01	NS	NS	NS	<0.05
2 : 3	NS	NS	<0.05	<0.05	<0.05	<0.05

n = Number of cases in each group.

TABLE II– *Fetal IgG (mg/dl) Levels According to Mode of Delivery in Normal Pregnancy and Pregnancy Associated Hypertension*

Mode of delivery		Normal pregnancy	Pre-eclampsia and eclampsia	Pregnancy with essential hypertension
I. Vaginal				
(*a*) Normal		1514.2 ± 225.60 (n =45)	1426.23 ± 301.78 (n =14)	1389.32 ± 421.35 (n = 38)
(*b*) Forceps		1245 (n = 1)	1189.24 ± 226.71 (n = 10)	– –
II. Cesarean		1290 (n = 2)	1213.16 ± 275.28 (n = 6)	1236.6 ± 14.67 (n = 8)
p value	Ia : Ib	<0.001	<0.001	–
	Ia : II	<0.001	<0.001	<0.05

n = number of cases in each group.

TABLE III– *Relationship Between Ig Levels (mg/dl) in cord Sera and Birth Weight*

Weight (kg)		IgG	IgA	IgM
	Normal	1434.8 ± 270 (n = 9)	28.3 ± 10.4 (n = 2)	48.4 ± 24.77 (n = 3)
2.0-2.5	PAH	1336.3 ± 192 (n = 17)	23.4 ± 4.4 (n = 8)	48.6 ± 2.5 (n = 6)
	Normal	1321.33 ± 341.76 (n = 21)	23.2 ± 3.80 (n = 10)	45 ± 1.8 (n = 8)
2.6 - 3.0	PAH	1343.2 ± 223.3 (n = 39)	21.4 ± 6.1 (n = 18)	48.4 ± 3.2 (n = 15)
	Normal	1420.89 ± 348.16 (n = 18)	23.4 ± 1.8 (n = 5)	49.5 ± 0.9 (n = 6)
3.1-3.5	PAH	1396 ± 211.2 (n = 20)	21.9 ± 8.2 (n = 7)	46.8 ± 1.4 (n = 5)

p value amongst each subgroup is not significant.
n = number of cases in each group.

in the feto-placental vascular system particularly in umblical vein, thereby causing ultrafiltration of proteins in the fetal venous system leading to an increase in their concentration in cord blood.

IgA and IgM were detected in the cord blood of newborns of mothers with normal pregnancy and PAH in 40.3 and 34.7% cases, respectively. Gupta *et al.*(15) have found IgA in 66% of cord blood samples and IgM in all cases of normal pregnancy attributing these higher levels to high endemicity of parasitic and bacterial infections in our country. In the present study significantly higher levels of IgA and IgM in newborns of mothers having pregnancy with pre-eclampsia and eclampsia could be explained by a history of infection due to premature rupture of membranes, repeated per vaginum examinations, interference by Dai, and prolonged labor in such cases. On the contrary Misra *et al.*(13) could not detect IgA and IgM in cord blood. IgA present in the cord blood is produced by the fetus in response to various intrauterine antigenic stimuli(5,6). It is, therefore, thought to be of potential importance for detection of intrauterine infection, since it does not vary with the period of gestation and birth weight(16). In the present study, IgG, IgA and IgM showed no correlation with gestational age as the babies were born between 37 to 40 weeks gestation. Cederquist *et al.*(16) have showed that IgM concentration during week 40 were significantly higher than those during weeks 27 to 37, but not significantly different from IgM levels during weeks 38 to 39. IgG levels during weeks 38 to 42 were significantly higher than those during weeks 27 to 37. IgA did not vary with gestational age. Misra *et al.*(13) found a rise in mean IgG with increasing gestational age, reaching a peak at 41 weeks gestation.

We did not find any correlation of Ig levels with fetal weight, as the weight of newborns in our study ranged from 2.0 to 3.5 kg. However, Cederquist *et al.*(16) found significantly lower levels of IgM and IgG in fetuses weighing 2.0 kg and below when compared with those weighing between 2.5 to 4 kg.

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