

A STUDY OF SERUM IMMUNOGLOBULINS IN PREGNANCIES WITH HYPERTENSION AND TOXAEMIA

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SUMMARY

Forty-four pregnant women, 22 cases of pregnancy with pre-eclampsia and 11 patients of pregnancy with essential hypertension, all in their third trimester of pregnancy were selected. All of them were investigated.

Serum IgG, IgA and IgM were estimated in all cases by Single Radial Immunodiffusion method of Mancini *et al* (1965). Serum IgG shows a significant fall in pregnancy complicated with hypertension and toxæmia from normal pregnancy, but serum IgA and IgM show no significant change in these conditions.

Introduction

It has been observed by many workers like Kohelar and Farr (1966), Lerner and Dixon (1966), Mendenhall (1970), Song *et al* (1970), Benster and Wood (1970) and the present authors (1983) that there is a marked fall in the level of serum immunoglobulins during pregnancy. This fall is solely due to reduction in the level of serum IgG, as there is selective transplacental passage of IgG from mother to foetus. This fall is more pronounced when pregnancy is complicated with toxæmia, anaemia, essential hypertension or nephritis. These conditions add an extra pathological stress to the mother in addition to the already existing physiological stress i.e. pregnancy.

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Accepted for publication on 17-6-1983.

In the present study, the authors have tried to study the effect of essential hypertension and pre-eclamptic toxæmia on the serum immunoglobulins in third trimester of pregnancy by comparing the levels of immunoglobulin G, A, and M in normal pregnancy with those of pregnancy with hypertension and toxæmia.

Material and Methods

The cases were selected from outpatient department as well as admitted indoor patients from the department of obstetrics and gynaecology, Patna Medical College Hospital. Seventy-seven patients all in third trimester of pregnancy were included in the present study. Out of 77, 44 women had normal pregnancy without any complication. They were considered as control subjects. Out of the rest 33 subjects, 22 had pregnancy complicated with toxæmia. Their blood pressure was rang-

ing from 140/90 mm of Hg to 180/120 mm of Hg. They had either associated albuminuria of mild to severe degree or oedema feet alone or both of these two. Rest 11 patients were put in the group of essential hypertension, as they were either known cases of hypertension even before pregnancy or it was detected in the first half of the pregnancy. They had neither albuminuria nor oedema feet. Their blood pressure was ranging from 150/90 mm Hg to 190/130 mm Hg. Case history of every patient was taken in detail. All previous available records were noted.

Clinical examination and routine investigations such as Hb% estimation, R.B.C. count, routine examination of urine, blood pressure recording were done in all cases.

Quantitative determination of immunoglobulin G, A and M was done by "Single Radial diffusion method" of Mancini and Carbonara *et al* (1965). For this, specific tripartigen immunodiffusion plates for IgG, IgA and IgM were obtained from Behring Institute, Frankfurt through Hoechst Pharmaceuticals Ltd., Bombay.

The samples of sera of patients were placed in capillary tubes provided with

the plates in the partigen wells of all three immunodiffusion plates. Antigen-antibody precipitate rings were formed in a concentric manner around antigen wells. The diameters of precipitate rings of immunodiffusion plates for IgG and IgA were measured by travelling microscope after a minimum of 50 hours and of plates for IgM after 80 hours. The concentration of immunoglobulins related to measured diameters was recorded directly from the Tables of Reference Values supplied by Behring Institute. Sera used for determination of IgA and IgM were undiluted, but for IgG sera used were diluted 1:10 with isotonic saline. Therefore, the value of IgG was multiplied by 10, to get the correct value.

Observations

The comprehensive basic data obtained from the experiments are presented in Table I. This Table shows the average values, standard deviations and the range of primary data for all the three immunoglobulins IgG, IgA and IgM in the control group of normal pregnant women, pregnant women with essential hypertension

TABLE I

Serum Immunoglobulin G, A and M Concentration in Normal Pregnancy, Pregnancy With Hypertension and Toxaemia

State of Health	No. of observations		Serum IgG in mg per 100 ml.	Serum IgA in mg per 100 ml.	Serum IgM in mg per 100 ml.
Normal pregnancy	44	Average	1055.00	247.29	213.10
		S.D.	48.40	40.86	37.52
		Range	824-1208	184.1-341.1	155.9-346.0
Pregnancy complicated with essential hypertension	11	Average	984.82	325.60	218.70
		S.D.	80.45	41.28	35.45
		Range	852-1113	173.1-303.3	175.5-257.2
Pregnancy complicated with pre-eclamptic toxaemia	22	Average	827.70	224.27	231.40
		S.D.	53.06	55.78	56.72
		Range	755-932	170.50-315.00	194.0-356.1

and pregnant women with pre-eclamptic toxæmia.

Table II to Table VII show statistical parameters of comparison namely, standard deviation (S.D.), Standard error (S.E.), experimental (t) and tabular value at 90% confidence limit ($t_{0.1}$) of student's t test. These Tables show whether the changes in the values of IgG, IgA and IgM are significant or otherwise from a rigorous statistical standpoint.

The change in the level of IgG from the control group to pregnant women with hypertension can be seen in Table II. Since $t_{0.1}$ (tabular) is less than t for the experimental data, the change is significant. The average value of IgG has changed from 1055.0 in the control group to 984.8 in women with essential hypertension.

Table III shows that although the average value of IgA in pregnant women with hypertension (235.0) is less than that in the control group (247.29), in a rigorous statistical analysis, there is not a significant change. Similarly, Table IV demonstrates that the change of IgM level from control group (213.1) to pregnancy with hypertension (218.7) is also not significant.

It can be seen from Table V that the average level of IgG in women with pre-eclamptic toxæmia (827.7) is much lower than the level in the control-1 group (1055.0). At the same time the statistical analysis also shows that this change is highly significant. Table VI demonstrates that the change in the level of IgA in pregnancy with pre-eclamptic toxæmia

TABLE II

Serum IgG Concentration in Normal Pregnancy and in Pregnancy, Complicated With Hypertension

State of Health	No. of observation	Serum IgG in mg per 100 ml	S.D.	S.E.	t experimental	(tabular)	Remarks on change
Normal pregnancy	44	Average	1055.00				
		Range	824-1203	98.40	20.90	2.19	1.67
Pregnancy with hypertension	22	Average	984.82				
		Range	852-1113	80.45	24.26		

TABLE III

Serum IgA Concentration in Normal Pregnancy and in Pregnancy Complicated with Hypertension

State of Health	No. of observations	Serum IgA in mg per 100 ml	S.D.	S.E.	t (experimental)	$t_{0.10}$ (tabular)	Remarks on change
Normal pregnancy	44	Average	40.86	8.67			
		Range	184.10-341.1			0.77	1.67
Pregnancy with hypertension	11	Average	41.38				
		Range	173.1-303.3		12.47		

TABLE IV
Serum IgM Concentration in Normal Pregnancy and in Pregnancy Complicated With Hypertension

State of Health	No. of observations	Serum IgM in mg per 100 ml	S.D.	S.E.	t (experimental)	t _{0.1} (tabular)	Remarks on change
Normal pregnancy	44	Average 213.10 Range 184.1-341.1	37.52	8.02	0.58	1.67	not significant
Pregnancy Complicated with hypertension	11	Average 218.70 Range 175.5-257.2	29.82	8.99			

TABLE V
Serum IgG Concentration in Normal Pregnancy and in Pregnancy Complicated With Pre-eclamptic Toxaemia

State of Health	No. of observations	Average and range of serum IgG in mg per 100 ml	S.D.	S.E.	t (experimental)	t _{0.1} (tabular)	Remarks on change
Normal pregnancy	44	Average 1055.00 Range 824.1203	98.40	20.90	9.33	1.64	Highly significant
Pregnancy with PET	22	Average 827.70 Range 755-932	53.06	15.96			

TABLE VI

Serum IgA Concentration in Normal Pregnancy and in Pregnancy Complicated With Pre-eclamptic Toxaemia

State of Health	No. of observations	Serum IgM in mg per 100 ml	S.D.	S.E.	t (experimental)	t 0.1 (tabular)	Remarks on change
Normal Pregnancy	44	Average 247.30 Range 184.10-341.1	40.86	8.67			
Pregnancy with PET	22	Average 224.27 Range 170.50-315.00	55.78	10.80	1.60	1.64	Not significant

TABLE VII

Serum IgM Concentration in Normal Pregnancy and in Pregnancy Complicated With Pre-eclamptic Toxaemia

State of Health	No. of observations	Serum Igm n mg per 100 ml.	S.D.	S.E.	t (experimental)	t 0.1 (tabulated)	Remarks on change
Normal pregnancy	44	Average 213.10 Range 184.10-341.1	37.52	8.02			
pregnancy with PET	22	Average 231.40 Range 194.0-356.1	55.72	17.10	0.96	1.64	Not significant

(224.27) is not significant in comparison with that in the control group (247.3).

Similarly, Table VII demonstrates that the change in the level of IgM from the control group (213.10) to pregnant women with pre-eclamptic toxæmia (231.40) is also not significant.

Discussion

Immunoglobulin G

The mean serum immunoglobulin G level in the present study shows a very significant fall from the group of normal pregnancy to the group of pregnancy with hypertension and further to pre-eclamptic toxæmia.

Horne *et al* (1970) found serum IgG level to be 811 mg per 100 ml in pregnancy with hypertension, which fell to 747 mg per 100 ml when proteinuria developed. They found that level of IgG in the sera of hypertensive pregnant women was always lower than that of the normal pregnant women, but it was higher than that of the pre-eclamptic group. Benster *et al* (1970) and Burdash *et al* (1973) also observed similar trends.

Hardie and Kench (1967, 1969) and Benster *et al* (1970) have suggested that the immunological process involved in pregnancy with toxæmia is different from that of the normal pregnancy per se. Apart from the theory of different immunological processes involved in pregnancy with toxæmia, a depression of IgG synthesis or the formation of immune complexes can be a possibility for the lowering of the level of IgG. The profound endocrinological changes of pregnancy and of pre-eclampsia could be responsible for the suppressed immunological status of mother (Burdash *et al*, 1973).

A more convincing explanation for the lowering of the level of IgG in toxæmia can be the loss of IgG in the urine. This

view has been supported by McEwan (1968), Horne *et al* (1970) and Studd (1971). Studd *et al* (1970) observed a decrease in low molecular weight proteins and an increased concentration of high molecular weight proteins in patients with toxæmia.

This indicates retention of macroglobulins, too large to be filtered and molecular sieving of intermediate and low molecular weight proteins in the urine through the defective glomerular basement membrane. Horne *et al* (1970) have shown that pre-eclamptic patients with moderate or severe proteinuria had more depressed level of serum IgG than those without or with very mild proteinuria. Possibly the depression of serum IgG is proportional to the daily loss of protein in the urine.

Immunoglobulin A

Serum IgA level shows a very small variation in the present study, which is not significant. McEwan (1968), Studd (1971) and Burdash *et al* (1973) also did not find any significant variation in the concentration of serum IgA in these conditions.

McEwan (1968) demonstrated IgA molecules in concentrated urine of the patients with severe hypertension and pre-eclampsia. The molecular weights of IgG and IgA are similar. Hence IgA molecules may pass in the urine through defective glomerular basement membrane as IgG molecules pass, thus resulting in a reduction in its serum level. But no significant fall could be found in serum IgA level even in severe hypertension and proteinuria. This may be due to the fact that the higher turnover of IgA than that of IgG even in toxæmia and hypertension may be able to maintain the IgA level.

Immunoglobulin M

In the present study there is no significant variation in the level of serum IgM

concentration in hypertension and toxæmia from that of normal pregnancy. Studd (1971) and Burdash *et al* (1973) also had made similar observations.

Acknowledgement

The authors are grateful to the Superintendent, Patna Medical College Hospital, Patna, for permission to publish the hospital data.

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