CLINICAL STUDY AND THE RESPONSE OF LYMPHOCYTES TO PHYTOHAEMAGGLUTIN IN WOMEN WITH ECLAMPSIA/PREECLAMPSIA

By

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SUMMARY

From our study it was thus concluded that severe pre-eclampsia was common in young primis conceiving during first year of marriage. There was increased perinatal loss as severity of pre-eclampsia increased. IUGR was a common complication. Low birth weight and low placental weight was also a common accompaniment as severity of pre-eclampsia increased. This could be well related to the increased serum mucoprotein levels in blood and decreasing maternal T lymphocytes (Supressor). Rather pre-eclampsia was severe with poor foetal outcome in patients who had decreased T cells and raised SMP levels. Thus the severity of pre-eclampsia whether in terms of need for early intervention or of low birth weight baby may be related to the blood serum muco-proteins and maternal T cell levels.

Introduction

Since the beginning of this century several hypothesis have been proposed associating a breakdown of maternal immunological tolerance to the fetus and the onset of pre-eclampsia. Chesley (1978) stated that many familial factors are operative. Liston 1979 claimed that patients develop PE—by autosomal recessive inheritance. Jenkins (1973) found increased HLA matching between PE + patients and their husbands emphasising immunogenic hyporesponsiveness of PET mothers.

The immune response is mediated by cellular (T cell function) and humoral (B cell) mechanisms. It is generally accepted that T cell function measured by nitrogenic response to phytohaemagglutinin (PHA-M) is reduced in pregnancy. The primary lesion in PET lies in altered T cells, because their defective component cannot respond to the first challenge of paternal antigens, although they can function normally in later pregnancies. Antigen (Fetus and Placental tisue itself) is common in population and Antigen-Antibody reaction normally does not occur due to supressor of T cells.

Serum mucoprotein (SMP) subfraction responds more to the immune stress. SMP is probably immuno suppressive *in vivo* also with increasing immunogenic dysparity between feto-placental unit and the host. SMP levels in blood of PET

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patients are raised with poor foetal outcome. This study conducted at Govt. Medical College, Nagpur correlates the foetal outcome in toxaemia group to maternal hyporesponsivenss and SMP levels in blood.

Material and Methods

A total of 70 cases attending O.P.D. and those admitted in Gynaec. and Obstetric wards were included in the study.

A detailed clinical history was recorded and clinical examination was done. Patients suffering from other diseases like infections and septicaemic illnesses were excluded from the study.

The cases were classified as follows:

Group A — Control Cases (25)
- A1 — Normal Pregnancy, non-hypertensive cases—13
- A2 — Normal nonhypertensive, non pregnant cases—12.

Group B — Cases of PET (45)
- B1 — Patients with mild PET—16
- B2 — Patients with severe PET—16
- B3 — Patients with eclampsia—13.

Following investigations were done:
1. Haemoglobin estimation
2. Urine-microscopy, albumin, sugar, culture and sensitivity
3. Blood urea and blood creatinine
4. Fundoscopy.

Special Investigations for Immunological Assessment

1. Absolute Lymphocyte count
2. Serum Seromucoid Factor (Winzler's 1955)
3. Blastoid transformation of lymphocytes (Pentycross 1968)

In short, lymphocytes were separated from heparinized blood by Diacoll (Decruz Laboratories, Bombay). Twin cultures were set up in minimum essential medium (MEM-Bagle). In culture A-25% of autologous serum was added and in culture B-25% of human AB serum was added. 0.1 ml of phytohaemagglutinin (PHA-M) Difco Laboratories, (U.S.A.) was added to each culture tube. Cultures were incubated at 37°C for 72 hours.

Cells were harvested, smears done and stained by Giemsa's stain. Total of 500 cells were scored under oil immersion lens and were classified as 'Blast' cells and untransformed lymphocytes according to caron's criteria (1969).

Observations

Thus in severe PET/eclampsia patients had raised SMP levels, decreased mitogenic response, low birth weight, low placental weight, and increased perinatal mortality (28.8%) as compared to normal pregnancy controls. The absolute lymphocyte count was not altered in both the groups.

Discussion

In our study group mostly the eclampsia patients were young primigravidae conceived during the first year of marriage. In multigravida, toxaemia was less severe. In booked antenatal patients the disease was milder and progress was checked by early and effective management in hospital. In control group IUGR was not seen. In study group IUGR complicated in 26.6% patients.

In control group SMP level was significantly raised in pregnant patients, as compared to A2-nonpregnant patients.

TABLE I

Correlation of Foetal Outcome to Mean SMP level, Lymphocyte Count and Mitogenic Response of T. Cells

Group	Male: Female Ratio	Live Birth	Fresh Still birth	Macera-ted Still birth	Neonatal death	Mean Birth wt. kg.	Mean placenta wt. gms.	Mean SMP Mg%	Mean count/cms	Mitogenic Plasma +	Response Plasma —
A1	7:6	13	—	—	—	2.7	270	125.4	3746	60.9%	62.8%
A2	—	—	—	—	—	—	—	111.1	2700	59.6%	61.7%
B1	8:8	16	—	—	—	2.6	256	142	3450	51.2%	60.5%
B2	10.6	8 (50%)	4 (25%))	1 (6.25%)	3 (18.75%)	1.8	236	159.3	3262	41.4%	55.7%
B3	7:6	8 (61.4%)	2 (15.5%)	1 (1.6%)	2 (15.5%)	1.93	204	179.7	3357	36.6%	50.6%

TABLE II

Level of SMP and Result of Paired T. Test

Group	No. of Patients	SMP (mg%) Mean ± S.E.	Range	S.D.	Paired pairs	T. test No. (n-1) observa-tions	P. Value	Significance
A1	13	125.46 ± 0.072	110-140	7.46	A1 : B1	28	<0.001	Significant
A2	12	111.16 ± 3.479	92-132	12.4	11 : B2	28	<0.001	Significant
B1	16	142.125± 4.244	116-170	16.977	A1 . B3	25	<0.001	Significant
B2	16	161.125± 8.672	120-230	34.691	A1 : A2	24	<0.001	Significant
B3	13	179.69 ± 7.990	130-240	28.767			—	

SMP level was significantly raised in PET group as compared to normal pregnant patients. Eclampsia patients showed more increase as compared to mild PET group. Similar results were quoted by Good *et al*, 1973; Need, 1976. Since SMP level increases in immunologic stress probably increasing immunogenic dysparity in PET provokes increase in SMP levels. SMP levels are therefore helpful in clinical correlation and management of patients.

The absolute lymphocyte count was done to obviate the possibility of getting immunosuppression by obvious reduction in absolute lymphocyte count. However the count remained more or less same in both groups.

The mitogenic response of maternal T cells decreased significantly in both eclampsia and severe PET groups when compared with pregnant and non-pregnant controls irrespective of the presence or absence of autologous plasma in culture medium. The lymphocytes of patients with severe PET or eclampsia showed a greater hyporesponsiveness to PHA. In mild PET group a significant hyporesponse was observed only when maternal plasma was in the culture. Otherwise lymphocytes behaved

TABLE III (A)
Mitogenic Response in Various Groups

Group	No. of patients	Plasma (+)			Plasma (—)		
		Range	Mean	S.D.	Range	Mean	S.D.
A1	13	46-68	60.9	5.95	52-68	62.3	4.619
A2	12	53-64	59.66	2.98	53-67	61.75	3.851
B1	16	48-65	51.2	6.274	52-67	60.5	4.422
B2	16	0-62	41.4	17.79	45-65	55.7	7.453
B3	13	0-60	36.6	14.88	32-62	50.6	8.948

TABLE III (B)
Result of Paired T. Test

Sr. No.	Maternal	Plasma (+)	P. Value	Maternal plasma (—) (P. value)	
1. Normal	Pregnant:	Non-pregnant	>0.05 (NS)	>0.05—(NS)	(NS—Not significant) (S—Significant)
2. Normal	Pregnant:	Mild PET	<0.05 (S)	>0.05—(NS)	
3. Normal	Pregnant:	Severe PET	<0.05 (S)	<0.05—(S)	
4. Normal	Pregnant:	Eclampsia	<0.05 (S)	<0.05—(S)	
5. Mild PET		Eclampsia	<0.05 (S)	<0.05—(S)	
		The Effect of Own Plasma			
6. Normal Pregnant Plasma (+ : Plasma (—)			>0.05 (NS)		
7. Eclampsia Plasma (+ : Plasma (—)			<0.05 (S) >0.01 (NS)		

similar to those of normal pregnant patients in absence of the autologous plasma in culture. The eclampsia patients showed a significant hyporesponse as compared to mild PET group. Thus there was a significant hyporesponsiveness to PHA in sévere PET and eclampsia patients. While comparing the immunosupressive effect of autologous plasma in normal pregnant and eclampsia, the presence of plasma in culture medium significantly decreased the mitogenic response in eclampsia group, but not in normal pregnancy. Plasma seems to be more immunosuppresive in eclampsia.

Reduction in the blastoid transformation response to P.H.A. with severe toxaemia and eclampsia indicated deficiency of T lymphocytes. It is probable that the supressor fraction of T. cells is reduced in PET and eclampsia. This, therefore, will result in breaking of immune tolerance and poor foetal outcome.

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