SERUM IMMUNOGLOBULINS IN NORMAL AND INTRAUTERINE GROWTH RETARDED NEONATES AND THEIR MOTHERS

By

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SUMMARY

Immunological system in man is known to develop largely before birth. Intrauterine nutritional deprivation is bound to affect the Immunocompetence of such a neonate. A study was therefore undertaken to evaluate the immunological effects of intrauterine growth retardation in forty five full term neonates with birth weight less than 2.5 Kg. The results were compared with ten full term neonates weighing more than 2.5 Kg at birth.

Intrauterine growth retarded neonates were observed to have significantly lower levels of immunoglobulin G as compared to their corresponding mothers while normal weight neonates had significantly higher levels of immunoglobulin G in comparison to their corresponding mothers. Serum immunoglobulin A was detected in almost similar percentage of the neonates of the two groups. Serum Immunoglobulin M was detected in all neonates. 4.44% of intrauterine growth retarded neonates had elevated levels of serum immunoglobulin A and M, indicating some kind of intrauterine infection leading to intrauterine growth retardation.

No significant difference was observed in the maternal serum immunoglobulin levels in the two groups.

Introduction

Malnutrition contributes to intrauterine growth retardation. Balanced nutrition is essential for a good immune response of the body. Abnormalities produced by prenatal intrauterine malnutrition are much more severe and long lasting than those resulting from malnutrition after birth (Chandra *et al*, 1974). Estimation of serum immunoglobulins in intrauterine growth retarded neonates and their mothers was undertaken to look into this aspect of the problem.

From: Lady Hardinge Medical College and Associated Hospitals, New Delhi.

Accepted for publication on 24-2-87.

Material and Methods

The study included 55 neonates and their corresponding mothers. The neonates included were of more than 37 weeks of gestation.

The mothers with any obvious infection, premature rupture of membranes and any obvious cause leading to intrauterine growth retardation were exclud-

ed from the study. The pairs were divided into two groups.

I. Test Pairs: This included neonates with birth weight less than 2.5 Kg and their corresponding mothers.

II. Control Pairs: This included neonates with birth weight more than 2.5 Kg and their corresponding mothers.

Serum immunoglobulins were quantitated by Single Radial Immunodiffusion method using immunodiffusion Tripartigen plates (Hoechst-Pharmaceuticals Ltd.). These plates contain a prepared agar gel in which H-Chain specific antiserum to the respective immunoglobulin is incorporated. The assay values for IgG, IgM and IgA were determined with reference to WHO international immunoglobulin reference preparation 67/86.

Fetal blood was collected from the severed placental end of the cord, after delivery of the fetus. Maternal venous blood was collected from the antecubital vein during parturition.

Observation

The test neonates were observed to have significantly lower ($p < 0.001$) levels of serum IgG when compared to their corresponding mothers while these were statistically significantly higher ($p < 0.05$) in normal weight neonates, when compared to their corresponding maternal levels. In 66.67% of test neonates, serum IgG was lower, in 20% it was equal and in 13.33% it was higher than the corresponding maternal levels. Amongst control neonates, 80% of them had higher, 10% had equal and 10% had lower level of serum IgG than their mothers. There was no statistical difference in the serum IgG levels of the test and control mothers.

TABLE I

Serum Immunoglobulin Levels (Mg%) in I.U.G.R. Neonates (N) and Their Mothers (M)

	IgG		IgA		IgG	
	M	N	M	N	M	N
Mean	1606.61	1398.85	267.05	57.10	253.19	43.60 (100% Positive)
SD	260.21	233.50	33.60	22.22% (cases Positive)	50.85	
Range	960.51 to 2225.60	980.67 to 1966.20	118.09 to 335.89		114.76 to 435.58	

TABLE II

Serum Immunoglobulin Level (Mg%) in Normal Weight Neonates (N) and Their Mothers (M)

	IgA		IgM		IgM	
	M	N	M	N	M	N
Range	1651.16	1899.64	250.91	54.37 (+ve in 30% cases)	259.75	28.86
SD	247.84	205.73	30.47		55.23	(100% +ve)
Range	1157.30 to 2225.60	1402.40 to 2225.60	143.10 to 335.89		125.20 to 427.87	

Serum IgA was detected only in 22.2% of the test neonates and 30% of the control neonates. Serum IgM was detected in all neonates. 28.86 mg% is the least amount of serum IgM that can be measured by the Tripartigen plates. 84.5% of test neonates and all control neonates had levels less than 28.86 mg%. In the test neonates, 4.44% of neonates showed raised levels of both serum IgM and IgA. Their mothers were also observed to have relatively higher levels of serum IgA and serum IgM. But the values were within two standard deviation of the mean. The serum IgG of these maternal neonatal pairs were within normal limits. No statistical difference was observed in the serum IgG, IgA and IgM levels in the mothers of the two groups.

Discussion

Lower levels of serum IgG in intrauterine growth retarded neonates could be the cause of increased risk of infections leading to increased morbidity and mortality in them. In the test group 66.67% of neonates had serum IgG values significantly lower ($p < 0.001$) than their corresponding mothers while 80% of control neonates had higher levels ($p < 0.05$) of serum IgG than their mothers. These findings are in agreement with Raghvan *et al* (1976), Paramjeet *et al* (1979) and Haridas *et al* (1983). Immunoglobulin-G in fetal serum is transferred across the placenta both by an active and a passive process (Gitlin *et al*, 1964). To some extent, it is also synthesised in the fetal spleen, where it begins at twelve weeks of gestation (Steihm and Richard 1975). As a result of the passive transfer of serum IgG across the placenta, fetal IgG remains propotional to maternal IgG. The mechanism undergoes maturation with increasing age to permit increased transfer of serum IgG across the placenta. The second is an active enzymatic process that actively transfers maternal IgG to the fetus. This process is inhibited at a higher maternal IgG levels and is increasingly activated at low maternal serum IgG levels and thus it serves to bring to normal fetal serum IgG levels, even when maternal levels are low. In cases of placental insufficiency causing intrauterine growth retardation, these mechanisms are impaired resulting in lower fetal levels, even though maternal levels are within normal limits. Young *et al* (1968) have suggested that in severe placental insufficiency, immunoglobulin-G globulin like glycogen is more severely depleted than other body constituents. Chandra *et al* (1975), Raghvan *et al* (1976) and Paramjeet *et al* (1979) have suggested that as malnutrition has an influence on the immune system of the body, similarly intrauterine malnutrition decreases immune response and hence serum IgG levels in these neonates. This may lead to higher incidences of neonatal infections in these neonates as compared to normal weight neonates.

The levels of serum IgG were similar in the mothers of the test and control neonates.

Serum IgA was detected in 22.22% of the test neonates and 30% of control neonates Immunoglobulin A, although of similar size and sedimentation constant (7S) as IgG, does not crosss the placenta and is rarely detectable in the sera of the normal term fetuses, Thom *et al* (1967). Raghavan *et al* (1976), detected serum IgA in the cord blood in 31% of low birth weight neonates and in 33% of full term normal weight neonates.

All neonates of both the groups showed

presence of serum immunoglobulin M. Gitlin *et al*, 1964, proved by their studies employing tagged IgM that it does not cross the placental barriers and therefore concluded that any demonstrable serum IgM in fetal blood was of fetal origin. Later this was shown by Prasad *et al* (1971) and Steihm and Richard (1975).

4.44% of test neonates had relatively higher levels of serum IgM and IgA than the mean values, indicating some kind of intrauterine infection which could be the cause of intrauterine growth retardation in these neonates.

No significant difference was observed in the serum IgM and IgA levels in the mother of the two groups.

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