SERUM PROTEINS INCLUDING IMMUNOGLOBULINS IN YOUNG FULLTERM PREGNANT FEMALES

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Over the years there have been many studies on the serum proteins of different adult population groups. Some of these have been carried out in pregnant females with a view to see its relation to the nutritional status of the mother as protein levels are considered to affect the growth in uterus and foetal outcome. The study of the immunoglobulins in adults has been taken up in this country quite recently and some reports have appeared (Gupta *et al*, 1972; 1975; Samuel *et al*, 1970). No specific study however has been conducted in young females during uncomplicated pregnancy or pregnancy complicated with infection. This study was therefore taken up and the results are presented here.

Material and Method

The test groups comprised of 31 healthy young pregnant females and 15 pregnant females who had some infection during their antenatal period. Ten non-pregnant young females were studied as a control. The age of the subjects in both test and control groups ranged between 18-35 years, all were on ordinary routine diet and belonged to the middle socio-economic status. Sera were obtained from the anticubital vein and in case of the pregnant subjects at the end of the second stage of labour. Total serum proteins were analysed by biuret method and protein fractions by paper electrophoresis (Fig. 1). Immunoglobulins were estimated by methods of single radial diffusion in agar gel containing antisera (Mancini *et al*, 1965). Concentration of these was graded against the standard sera obtained from the immu nology unit of W.H.O. (Fig 2).

Observations

The results of estimation of total proteins and its fraction obtained are tabulated below (Table I).

It is observed that the total proteins of all the groups fall almost into the same range with only a slight lowering of the levels in the infected pregnant group. Albumin levels of the pregnant normal as well as infected are significantly lower than the non-pregnant control. This lowered albumin level is compensated by a raised level of globulins in the pregnant subjects. The rise in globulins is almost

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TABLE I
Total Protein and its Fractions as gms.%

	Total protein	Albumin	Globulin
Pregnant (Normal)	7.25 ± 0.43	2.70 ± 0.34	4.48 ± 0.52
Pregnant (Infected)	6.94 ± 0.84	2.50 ± 0.63	4.44 ± 0.48
Non-pregnant	7.02 ± 0.10	3.03 ± 0.35	4.02 ± 0.17

the same whether the test subject is infected or not.

The globulins were further fractionated and the results are shown in Table II.

TABLE II
Different Fractions of the Globulins as gm.%

	$Alpha_1$	$Alpha_2$	Beta	Gamma
Pregnant (Normal)	0.86 ± 0.2	0.30 ± 0.12	1.56 ± 0.41	1.75 ± 0.48
Pregnant (Infected)	0.72 ± 0.21	0.35 ± 0.22	1.50 ± 0.30	1.84 ± 0.50
Non-pregnant	0.29 ± 0.19	0.64 ± 0.33	1.22 ± 0.27	1.72 ± 0.62

It will be observed that $Alpha_1$ and Beta are raised in the pregnant females as compared to the non-pregnant controls. Gamma globulin is only slightly raised in the infected pregnant females while it is almost the same in uncomplicated pregnant and non-pregnant females. $Alpha_2$ is lowered in pregnant in comparison with the non-pregnant females. $Alpha_1$ and Beta therefore show a specific rise and $Alpha_2$ a specific fall in the pregnant. On the other hand, Gamma globulin show no change in a uninfected pregnancy and rise only when a pregnant subject suffers from some infection.

The levels of three major immunoglobulins were measured and the results are given in Table III.

It will be observed that levels of immunoglobulin of both the test groups of the pregnant females are higher than the levels obtained in the non-pregnant controls. IgG is almost double of the non-pregnant levels in both the groups of pregnant females. IgM shows a three-fold increase in normal pregnant and more than four-fold increase in the infected pregnant females. IgA is only slightly higher in pregnant as compared to non-pregnant controls though the levels are higher in uncomplicated test group.

The greatest increase is seen in IgM, moderate in IgG and least in IgA.

This shows that all the immunoglobulins are increased in a pregnant state both uncomplicated or complicated with infection, the greatest increase being in IgM followed by IgG and IgA. As both the test groups of pregnant females show this change it can be considered specific. A

TABLE III
Levels of Immunoglobulins Given in I. Units

	IgG	IgM	IgA
Pregnant (Normal)	237 ± 145	271 ± 223	140.5 ± 110.5
Pregnant (Infected)	235 ± 168	434 ± 300	113 ± 100
Non-Pregnant	132 ± 111	98 ± 41	100 ± 39

higher IgM level in infected pregnant females can be explained on the basis of the infection these subjects suffered during the antenatal period.

Discussion

Present study has brought out some significant features of differences between the total protein, protein fraction and immunoglobulin levels of pregnant against non-pregnant females.

Total protein levels of the 3 groups are not significantly different except slight lowering seen in the infected group. This is against the general belief and observation of Ceryell *et al*, (1960) who observed a fall of 13% in mean total serum protein in pregnant females and explained it on the basis of haemodilution.

A change in albumin globulin ratio is however observed in the present study with lowering of the albumin and raising of the globulin levels. This change is specific as it is seen in both the test groups. The globulin on further fractionation has shown a significant rise in $Alpha_1$ and Beta fraction, slight rise in gamma fraction and a significant fall in $Alpha_2$ fraction in comparison to normal controls. This alteration in different fractions suggests an immunological redistribution, readjustment or an altered production of different globulin fractions in the pregnant state. Brown *et al* (1958) have reported an increase in Alpha and Beta globulins with a decrease in other fractions. This broadly agrees with the present findings except that a rise is observed in gamma fraction also in the present study. This latter finding may be peculiar to the subjects of Indian origin. Brown *et al* (1958) attributed the fall in other fractions to their being selectively transferred to the foetus.

The levels of immunoglobulins in healthy mixed population of different parts of this country is shown in Table IV and compared with the present observations.

TABLE IV

IgG, IgM and IgA level of Different Studies in Indians Given as mg.%

		IgG	IgM	IgA
1. Samuel et al. 1970 (Bombay)	+	1350	159.0	172.0
2. Sehgal and Aikat 1970 (Chandigarh)	+	1145.0 ± 339.0	144 ± 60.0	273 ± 119
3. Gupta et al. 1972 (Varanasi City)	+	1154.67± 191.25	157.43± 49.47	287.13± 86.2
4. Gupta et al. 1974 (Varanasi Sarnath)	+	1675.6 ± 344.80	149.5 ± 55.45	278.0± 86.2
5. Gupta et al. 1975 (Male Tibetans)	+	1290 ± 249.5	187.0 ± 76.2	284.7 95.0
6. Present study (Delhi) Females		2204 ± 1348	204 ± 168	146 ± 148
Pregnant (Normal)				
Pregnant (Infected)		218.5 ± 1562	324 ± 225	151 ± 1.34
Non-pregnant		1227.6 ± 1032	73.5 ± 30.75	134 ± 52

Levels of IgG are seen to vary from

1154 ± 191 to 1675 ± 344 mg%; IgM 144 ± 60 to 187 ± 76 mg% and IgA 172 to 287 ± 86 mg% in different studies. Little is known regards the immunoglobulin levels of pregnant females only two studies being available in the medical literature from abroad which have been compared with the present studies in Table V. No studies on pregnant females are available from this country, therefore no comparison can be drawn as far as Indian subjects are concerned. The results obtained in the normal non-pregnant control group of the present study are comparable to the results of studies on mixed population from different centres of this country (Table IV). The results obtained in the 2 test groups are significantly different. Thus IgG levels are double, IgM levels five fold and IgA levels only slightly higher than the control. In the infected test group the levels of IgG are same as in the uninfected test group but IgM levels are very much higher and IgA levels slightly lower. Thus in uncomplicated pregnancy both IgG and IgM levels are significantly raised and IgA insignificantly raised. In infected pregnancy group IgG and IgM are still higher and IgA level only slightly raised.

Considering that it is only the IgG which is transferred against a gradient through the placenta to the foetus a rise in this immunoglobulin is understandable. As other immunoglobulins are not transfered a rise in their levels is a specific alteration as far as the pregnant state is concerned. Studd *et al* (1970) observed a reduction in all the 3 immunoglobulins at 27 to 33 weeks of pregnancy however in late pregnancy IgG and IgA showed a steady level and IgM a rise. This does not fall with the results obtained in the present study. These workers also observed a higher IgM concentration in primigravidae and there was no significant difference between the IgG and IgA levels of primi and multigravidae. These workers therefore postulated that a higher level of IgM in pregnant state was possibly in response to the strong stimulus of the foetus which a primigravida specially faces for the first time. This stimulus in primigravida acts as a primary stimulus and successive pregnancies become less effective with respect to IgM synthesis. Clark *et al* (1971) on the other hand have observed a normal level of IgM in pregnant female whether primae or multigravidae. In the present study 3 each in primae, second and third gravidae group showed very high levels of IgM. Therefore the rise being in response to a primary stimuli does not stand.

In the present study levels of IgA in the test as well as control were less than the levels given for normal mixed Indian

TABLE V

Immunoglobulin levels as mg% in young pregnant female

Worker	IgG	IgM	IgA
Gusdon et al. 1969	1381	124	189
Studd et al. 1970	1039	157	154
Present study			
Pregnant (Normal)	2204 ± 1348	204 ± 168	196 ± 148
Pregnant (infected)	218.5 ± 1562	324 ± 225	161 ± 134
Non-pregnant	1227.6 ± 1032	73.5 ± 40.75	134 ± 52

population (Samuel *et al*, 1970; Sehgal and Aikat, 1970; Gupta *et al*, 1972, 74, 75). This suggests either a low level of IgA in Indian female or low levels during the late stages of pregnancy. The present study therefore clearly brought out some very specific alteration in the blood proteins specially immunoglobulins in Indian pregnant females.

Summary

This paper reports the levels of serum proteins with special reference to immunoglopulins in 46 young pregnant and 10 non-pregnant females between 18-35 years of age and belonging to middle socio-economic status. Total proteins were not altered, albumin showed a fall with a relative rise in the globulin levels. The levels of IgG were almost double, IgM almost five fold and IgA only slightly raised when compared to the levels obtained in corresponding controls. This suggests that levels of IgG, IgM and IgA rise during pregnancy. The fractions of globulins showed a rise in $Alpha_1$ and Beta and a fall in $Alpha_2$ levels. The level of gamma globulins remain same as in non-pregnant females only rising slightly in infected test subject. To the knowledge of the authors this study is the first of its kind from this country.

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References

1. Brown, D. F., Franklin, E. C. and Kunkel, H. G.: J. Lab. Clin. Med. **52**: 729, 1958.
2. Clark, H. G. M., Freeman, J. and Phillips, W. P.: J. Obst. & Gynec., Brit. Cwlth. **78**: 105, 1971.
3. Caryll, M. N., Beact, E. F., Robinson, A. R., Macy, I. G. and Mack, H. C.: J. Clin. Invest. **29**: 1559, 1950.
4. Gudson, J. P.: Am. J. Obst. & Gynec. **103**: 895, 1969.
5. Gupta, R. M. and Aikat, B. K.: Ind. J. Med. Res., **58**: 289, 1970.
6. Gupta, R. M., Gupta, I. M., Gupta, V. M. and Marwah, S. M.: Ind. J. Med. Res. **63**: 1058, 1975.
7. Longsworth, L. S., Cartis, R. and Penbroke, R. A.: J. Clin. Invest. **24**: 46, 1945.
8. Mencini, G., Garbonara, A. O. and Heremans, J. F.: Internal. J. Immunohem. **21**: 235, 1965.
9. Samuel, A. M., Deshpande, V. R. and Singh, B.: Ind. J. Med. Res. **58**: 56, 1970.
10. Sehgal, S. and Aikat, B. K.: Ind. J. Med. Res. **58**: 289, 1970.
11. Studd, J. W. W., Starke, C. H. and Blainey, J. D.: J. Obst. & Gynec. Brit. Cwlth. **77**: 511, 1970.

See Figs. on Art Paper II