A STUDY OF EFFECT OF PREGNANCY, AGE AND PARITY ON SERUM IMMUNOGLOBULINS

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SUMMARY

Pregnancy has a marked influence on serum immunoglobulin G which falls significantly in the late pregnancy.

Serum IgA and IgM levels show no significant variation during pregnancy. Serum IgG levels were not influenced by age, parity or socio-economic conditions. Serum IgM was observed to be significantly high in primigravidae than in multigravidae ($P < 0.05$) women. No effect of age or socio-economic background was found on Serum IgM.

Serum IgA level was higher in pregnant women over 25 years. It was observed that socio-economic status per se had no significant effect on immunoglobulin levels.

Introduction

The importance of plasma protein and the variation in its level during pregnancy have been studied since long, even before the beginning of the 20th century.

Immunoglobulins, the protein molecules having antibody property, are divided into three major classes, IgG, IgA and IgM. All have similar antigenic, structural and biological activities but they differ in amino-acid sequence as their antibody functions are highly specific.

They are almost absent in the sera of new born babies, except IgG which crosses the placental barrier, but by adulthood human body develops all immunoglobulins. They are found in serum, colostrum, urine and saliva etc. Certain physiological conditions as age, sex, pregnancy and lactation, and pathological conditions which affect the individual's immune system, can influence the levels of immunoglobulins.

During pregnancy the serum concentration of Immunoglobulins vary from those of non-pregnant women. Maternal age, parity and period of gestation also influence the levels of immunoglobulins. Published data from various studies are contradictory. The total serum immunoglobulin as determined by serum electrophoresis has been found diminished during pregnancy. Immunochemical studies of fractional immunoglobulin concentration have shown an increase in one in-

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stance, no significant change in other and decrease in third.

Hoffstorm (1910), Wilson (1916), Muslin (1916-17) observed an increase in the synthesis and metabolism of total proteins during pregnancy. On the contrary, majority of the reports show a reduction in total protein, more so during third trimester.

In the present work, an attempt has been made to observe the influence of pregnancy, maternal age, parity, and socio-economic conditions on the maternal immune system by estimating the concentrations of immunoglobulin G, A and M in healthy pregnant women and comparing them with those of the healthy non-pregnant women.

Material and Methods

The present work was done in the postgraduate laboratory of the department of Obstetrics and Gynaecology, Patna Medical College Hospital. The cases were selected from the out patient department, obstetric indoor and labour room of Patna Medical College Hospital. Sixty-six cases were included in this study, out of which 22 were healthy non-pregnant females of child bearing age and 44 were women in their third trimester of normal uncomplicated pregnancy. Proper case history including menstrual and obstetrical history of each case was taken. Each case was examined systematically. Investigations like Hb % estimation, blood pressure recording, physical, chemical and microscopical examinations of urine were done in every case to exclude complications like anaemia, toxaemia, hypertension, diabetes, nephritis etc.

Ready-made tripartigen immunodiffusion plates were used for quantitative determination of IgG, IgA and IgM by single Radial Diffusion method of Mancini et al (1965). The plates were obtained from Behring Institute Chemi-Export Kontor GmbH, Frankfurt through Hoechst Pharmaceuticals Ltd., Bombay.

One ml. of blood was drawn from the antecubital vein with a sterilised dry syringe and was immediately transferred to a dry sterilised test tube along its side. The test tube was placed in standing position to facilitate the separation of serum from the clot. The separated serum was transferred to another test tube and was centrifuged. The supernatant serum was used in the experiment.

Method

An agar plate having 12 small wells is prepared incorporating specific antigen throughout the agar. The patients' sera are put into 11 wells. Accuracy control serum supplied from the company was put into the 12th well. The patients' sera as well as the accuracy control serum used were diluted 1:10 with isotonic saline before using for estimating IgG. A diffusion into the agar forms rings of antigen-antibody precipitate around the wells. The diameters of precipitate rings of immunodiffusion plates for IgG and IgA were measured after 50 hours and for IgM after 80 hours by travelling microscope.

The concentrations of immunoglobulin related to the measured diameters were read directly from the table of Reference Values supplied by Behring Institute. The diameter of the ring is directly proportional to logarithmic value of the immunoglobulin concentration. IgA and IgM were determined using undiluted serum only, for the determination of IgG, the value of IgG was multiplied by 10 to take care of the dilution.

Observation

Concentrations of Serum IgG, IgA and IgM in mg/100 ml in non-pregnant and healthy pregnant women in their third trimester is shown in Table I.

Serum IgG concentration shows a significant fall in its level during pregnancy from its average concentration in normal non-pregnant subjects.

Serum IgA concentration also shows a trend of reduction in pregnancy, but statistically the reduction is not significant.

Serum IgM concentration tends to increase during pregnancy, but the rise is not significant.

The effect of age on serum immunoglobulin concentration is shown in Table II.

There is no significant effect of age on serum IgG and IgM concentrations. Serum IgA is significantly raised in women over 20 years than under 20 years.

The effect of parity on serum immunoglobulin concentration is shown in Table III.

TABLE I

Serum IgG. IgA and IgM Concentration in Non-pregnant and Healthy Pregnant Women

No. of Observation	State of health	IgG in mg per 100 ml		IgA in mg per 100 ml	IgM in mg per 100 ml
22	Non-pregnant	1490.5 ±63.10		270.32 ±44.17	200.7 ±12.37
44	Healthy pregnant	1055.0 ±98.40		247.29 ±40.86	213.10 ±37.52
			P <0.01	P = 0.5	P = 0.1

TABLE II

Serum Immunoglobulin Concentration in Relation to the Maternal Age (in mg/100 ml)

Age of mothers in year	No. of cases	IgG (Mg/100 ml)	IgA (Mg/100 ml)	IgM (Mg/100 ml)
Under 20 years	15	1008 ± 113.50	198.2 ± 19.8	230.05 ± 39.5
20-24 years	29	1077.6 ± 112.34	229.4 ± 26.18	227.7 ± 38.03
25 years & above	22	1060.3 ± 124.8	233.40 ± 11.67	243.28 ± 55.97

TABLE III

Serum Immunoglobulin Concentrations in Relation to Parity (in mg per 100 ml)

Parity	No. of cases	IgG (mg/100 ml)	IgA (mg/100 ml)	IgM (mg/100 ml)
Primigravida	26	1052.09 ± 73.73	260.78 ± 120.61	260.04 ± 44.16
Multigravida	18	1057.36 ± 110.93	256.52 ± 46.97	204.35 ± 56.34
		P = 0.5	P = 0.5	P <0.05

Serum IgM level shows a reduction in multipara while serum IgG and IgA remain unchanged.

Discussion

Normal human pregnancy is considered as a state where the foetus exists as an allograft or homograft between two genetically different members of same species. The foetus being an allograft on the mother, influences the maternal immune system, which may be reflected by the alteration in the concentration of different immunoglobulin. In the present study, levels of serum IgG, IgA and IgM were estimated in 22 non-pregnant (control group) and 44 pregnant women in the third trimester.

Observations suggest that the level of serum IgG is significantly lowered during pregnancy especially during third trimester. Pregnancy suppresses the concentration of serum IgG (Table I) Gitlin et al (1964), Kohelar and Farr (1966), B. Benster and Wood (1970), Maroulis et al (1971) also found lowering of serum IgG concentration in late pregnancy. Studd (1971), Chandra et al (1973) observed a marked reduction in IgG level in the third trimester.

On the other hand Mendenhall (1970) obtained a reverse trend. He found serum IgG level to be higher in pregnancy than that of non-pregnant. This variation in observation of different workers could be due to differences in the statistical treatment of the date and selection of patients and control group. A great difference may be found in the concentration of the serum immunoglobulin of unrelated individuals in different states of health, of different age and race. These factors should be considered in selecting the control group.

The exact mechanism of reduction of serum IgG in apparently healthy pregnant women is not yet established. It has been suggested that the profound endocrinological changes taking place during pregnancy could affect the immunological status of the mother. There is an increased secretion of steroids, human chorionic gonadotrophin and corticosteroids which have suppressive effect on maternal thymo-lymphatic system. Nelson and Hall (1965) discovered lymph nodes lacking discrete germinal epithelium during pregnancy and puerperium implying a deficient potential for cellular immunity, thus causing deficient immunoglobulin formation (Jones, 1971). The selective transplacental passage of maternal antibody to the foetus is a very important postulation which can cause lowering of immunoglobulin G in mother, as IgG is the only immunoglobulin which can cross the placental barrier. This passive transfer begins before mid-pregnancy. The foetal IgG level increases in correlation with the age of gestation (Jones and Payne, 1967) with lowering of the maternal immunoglobulin G which is more marked during third trimester.

Physiological hydraemia of pregnancy may have some dilutional effect on serum IgG concentration, but the concentration of other serum proteins has been found unchanged except albumin and IgG, which are found lowered during pregnancy.

Effect of maternal age on the serum IgG was not significant. Burdash et al (1973) found lower level of IgG in the sera of women below 25 years than above it.

Serum IgG level was found more or less constant in primi and mutligravidae.

No significant influence on serum IgG

was found due to different socio-economic conditions of the patients.

Immunoglobulin 'A'

The serum IgA level shows a fall during pregnancy though statistically not significant (P = 0.5). Gusdon (1969), Chull, S. Song (1970), Benster and Wood (1970) also did not find any remarkable change in the serum IgG levels in pregnancy.

Values of serum IgA obtained in the present series are in agreement with other workers. The level obtained by Maroulis et al (1971) was higher. This could be due to individual variations in patients. Studd (1971) Hobbes et al (1971), Cochran and Wood (1974) found a significant fall in the mean serum IgA level in pregnancy. They found the reduction to be directly proportional to the increased plasma volume of pregnancy i.e. physiological hydraemia.

Maternal age has got an influence on the serum IgA levels. It was higher in women aged 25 years and above than those under 25 years. Benster and Wood (1970) had similar findings.

In the present study no effect of parity could be found on serum IgA. Socio-economic conditions also do not influence it.

Immunoglobulin M

In the present study the levels of serum IgM show an increasing tendency during pregnancy but statistically it is not significant. Gusdon (1969), Mendenhall (1970), Song et all (1970) also did not find any significant change.

Benster and Wood (1970) obtained the mean serum IgM to be raised in the late pregnancy. They considered this selective increase in IgM due to increased production of this immunoglobulin in late pregnancy.

Best et al (1970) found a fall in serum IgM in mid-pregnancy which they considered to be due to physiological dilutional factor.

Studd (1971), Maroulis (1971), Burdash (1973), Cochran (1974) did not find any significant change in IgM during pregnancy.

No influence of maternal age was observed on serum IgM in the present series. Parity affects its levels. Serum IgM is significantly high in primigravida ($P < 0.05$).

Benster and Wood (1970) had suggested that successive pregnancies may become a stimulus of decreasing effectiveness with respect to IgM synthesis. It can be compared with the progressive attenuation of the response to antigen in a 'hyposensitization' process.

No significant influence of socio-economic factors was found on serum IgM level.

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