SERUM LIPIDS, BLOOD COAGULABILITY AND FIBRINOLYTIC ACTIVITY IN PREGNANCY

by

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Much importance has been stressed on the alteration in the plasma proteins and lipids during pregnancy, Brown, (1954) Coryell *et al,* (1950) MacGillivary and Tovey, (1957) Menon, *et al.* (1958) and Von-Studnitz (1955). It has been revealed that the level of beta fraction of the serum protein globulin is also significantly raised during pregnancy, Martinez and Mantilla, (1959) Khanijo and Jungalwalla (1963) and it is thought that this increase might be related to a lessening in the clotting mechanism, since it may exert a checking effect on the unavoidable excessive bleeding at the time of parturition. Spaet and Kinsell, (1953) Kishore (1963). Boyd (1935) and Scandrett (1963) are of the opinion that the lipids are altered during the gestation period and the majority of them are transported as blood lipoproteins in association with the beta serum globulins. Therefore, it is thought germane to determine the relationship between serum lipids and blood coagulability together with the fibrinolytic activity in the different stages of pregnancy.

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Material and Methods

In the present study 55 normal pregnant women belonging to the second and the third decades of life were selected from those attending the antenatal clinic of the Zanana Hospital, Udaipur. A preliminary clinical investigation was carried out to exclude the presence of liver diseases, renal dysfunctions, hypertension, cardiac disorders, diabetes mellitus, anaemia and toxaemia of pregnancy. Twenty-five non-pregnant female medical studients between the ages of 20 and 26 years volunteered for the control study. Care was exercised that no difference occured in the socio-economical status and dietary habits in the patients as well as the volunteers.

The fasting blood samples were collected from the left antecubital vein. Three ml. of blood was taken in an empty penicillin vial for separating the serum; 2 ml. blood was collected in a vial containing 0.5 ml. of 3.8%

sodium citrate solution for the plasma and 1.0 ml. blood was subjected to the study of coagulation time, which was determined by the method of Lee and White (1913). The method employed by Bandopadhyay and Banerjee (1963) for determining the total serum cholesterol, beta lipoprotein cholesterol and lipoprotein percentage was adopted. The technique described by Jain and Gupta (1966) was followed for the purpose of staining the serum protein strips. The fibrinogen was estimated by the method of King (1951). The method of Bidwell (1957), as modified by Biggs and MacFarlane, was followed in all essential details for determining the fibrinolytic activity of the collected blood samples.

Results

An insignificant increase in the levels of the total cholesterol, beta lipoprotein cholesterol and beta lipoprotein percentage has been observed during the first two trimesters of pregnancy as compared to those obtained in the volunteers. However, those levels are significantly increased during the third trimester. But, these values remain at a slightly lower level for about one week following parturition in comparision to those of the last trimester of the pregnancy. A significant lowering in the coagulation time and fibrinolytic activity is also observed during the third trimester of pregnancy and immediately following the termination of the pregnancy (postpartum period). On the other hand, the last trimester of pregnancy and the postpartum period have exhibited an increase in the fibrinogen level. The coagulation time, and the fibrinogen levels, however, remained significantly unaltered in the first two trimesters of pregnancy. The results are summarised in Table I.

Discussion

The increased values of total cholesterol, beta lipoprotein cholesterol and beta lipoprotein percentage in the third trimester of pregnancy are in close consonance with those of other workers Oliver and Boyd, (1955) Burt *et al.*, (1962) Mullick *et al*, (1964) Scandrett, (1963) Von Studnitz (1956) and Gupta *et al.*, (1967). However, Geinitz and Schild (1955) are of the opinion that no change takes place in the beta lipoprotein and cholesterol levels during any of the stages of pregnancy. The values of volunteers and in the first trimester of pregnancy do not differ significantly. But they start rising in the second half of the middle of second trimester and remain high for about a week during the postpartum period.

As pregnancy nears full-term a deficiency in the albumin takes place which satisfactorily explains an increase in serum lipid content, mostly in beta lipoproteins. It has been suggested by Scandrett (1963) that the albumin fraction carries lipoprotein lipase enzyme which is deficient in the third trimester of pregnancy, thus resulting in an increase in the serum lipoprotein level. The same author has also reported that there is a decrease in the non-esterified fatty acids in pregnancy. Thus, it appears that the high beta lipoprotein level may be due to the fall of non-esterified fatty acids as well as of albumin,

TABLE I

Serum lipids, coagulability and fibrinolytic activity in pregnancy

Investigations	Non pregnant women (25)	First trimester (15)	Second trimester (15)	Third trimester (15)	Postpartum 1st week (10)
Total Cholesterol mg./100 ml.	190 ± 3.68	189 ± 3.63	226 ± 8.25	256 ± 9.15	247 ± 9.5
'P' Value	—	0.8	.001	.001	.001
Beta lipoprotein Cholesterol mg./100 ml.	98.9 ± 1.6	100 ± 1.83	127 ± 2.12	153 ± 2.51	148 ± 2.81
'P' Value	—	0.8	.001	.001	.001
Lipoproteins %					
Alpha.	29.4 ± .38	27.6 ± .41	23.3 ± .48	15.8 ± .38	17.7 ± .54
'P' Value	—	.001	.001	.001	.001
Beta.	70.6 ± .38	72.4 ± .41	76.7 ± .48	84.2 ± .38	82.3 ± .54
'P' Value	—	.001	.001	.001	.001
Coagulation time in minutes & seconds.	5.10 ± .15	5.00 ± .15	4.30 ± .14	3.40 ± .13	3.45 ± .15
'P' Value	—	0.1	.001	.001	.001
Fibrinogen mg.%	200 ± 5.67	225 ± 6.25	309 % 7.47	355 ± 10.3	313 ± 10.7
'P' Value	—	.001	.001	.001	.001
Fibrinolytic activity %	62 ± .66	60 ± .76	46 % .84	32 ± .81	34 ± .9
'P' Value	—	.05	.001	.001	.001

Values are means ± Standard errors.

Figures in parenthesis indicate number of subjects.

indicating that there is either defective fat metabolism or deficient serum albumin level or hyper beta globulinaemia (Gupta *et al.* 1967).

The values of coagulability and fibrinolytic activity in the third trimester of pregnancy and in the first week of the postpartum period are in close agreement with those of other workers, Stamm, (1962) Alkjaersig, *et al.* (1959). However, findings of the present study revealed that there is no significant alteration in the first and second trimesters of pregnancy.

Coagulability and fibrinolytic activity have important roles in certain haemorrhagic conditions during pregnancy. Decrease in coagulation time and fibrinolytic activity prevent excessive haemorrhage during pregnancy and labour. Excessive increase in the fibrinolytic system must be regarded as pathological in contrast to the other probable physiological reactions. It involves not only lysis of the fibrin present but even more destruction of fibrinogen, Factor V, Factor VIII and to a lesser extent of prothrombin. The resulting breakdown products of fibrinogen can no longer be transformed by thrombin into fibrin on the one hand, but act

additionally as inhibitors of fibrinogen polymerization on the other hand Alkjaersig, *et al.* (1959).

It has been reported that B factor of plasma, thromboplastin and stable conversion factor are present in beta globulin Aggeler *et al* (1959), Owen and Mckenzie, (1954) and is supposed to be called plasma thromboplastin component (P.T.C.). This observation was further supported by the study of plasma electrophoresis of plasma proteins in relation to blood coagulation, Rosenthal (1955). Therefore, our findings of decrease in coagulation and fibrinolytic activity correspond with the findings of hyper-betaglobulinaemia and hyper-beta lipoproteinemia in the later months of pregnancy and in the first week of postpartum period.

Summary

Fifty-five normal pregnant women were studied for the estimation of total cholesterol, beta lipoprotein cholesterol, lipoprotein percentage, coagulation time, fibrinogen and fibrinolytic activity of blood.

These cases revealed a significant increase in the total cholesterol, beta lipoprotein cholesterol, beta lipoprotein percentage and fibrinogen content of the blood. However, lower values were observed in the coagulation time and the fibrinolytic activity of blood. The results have been discussed in the light of available literature.

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References

1. Aggeler, P. M., Spaet, T. H. and Emery, B. E.: Science. **119:** 806, 1954.
2. Alkjaersig, N., Fletcher, A. P. and Sherry, S.: J. Biol. Chem. **234:** 832, 1959.
3. Bandopadhyay, A. and Banerjee, S.: Proc. Soc. Exper. Biol. & Med. **112:** 372, 1963.
4. Bidwell, E.: In Human Blood Coagulation and its Disorders. Edited by Biggs, R. and MacFarlane, R. G., ed. 2. Oxford 1957, Blackwell Scientific Publications, p. 412.
5. Boyd, E. M.: Am. J. Obst. & Gynec. **29:** 797, 1935.
6. Brown, T.: J. Obst. & Gynec. Brit. Emp. **61:** 781, 1954.
7. Burt, R. L., Leake, N. H. and Donnenberg, W. N.: Am. J. Obst. & Gynec. **84:** 1081, 1962.
8. Coryell, M. N., Beach, E. F., Robinson, A. R., Macy, I. G. and Mack, H. C.: J. Clin. Invest. **29:** 1559, 1950.
9. Geinitz, W. and Schild, W.: Arzneimittel-Forsch. **9:** 470, 1955.
10. Gupta, A. N., Sarkar, A. K. and Chakravarti, R. N.: Am. J. Med. Sci. **253:** 469, 1967.
11. Jain, R. C. and Gupta, O. P.: Indian J. Med. Sci. **20:** 713, 1966.
12. Khanijo, S. and Jungalwalla, B. N.: J. Obst. & Gynec. India. **13:** 160, 1963.
13. King, E. J. and Wooton, I O. P.: Microanalysis in Medical Biochemistry, ed. 2, London, 1951. J. & A. Churchill Ltd.
14. Kishore, N. and Gupta, K.: J. Obst. & Gynec. India. **13:** 151, 1963.

15. Krishna Menon, M. K., Radha, P. D. and Ramaswamy, N.: Indian J. Med. Sci. **12**: 930, 1958.
16. Lee, R. I. and White, P. D.: Am. J. Med. Sci. **145**: 495, 1913.
17. MacGillivary, I. and Tovey, J. E.: J. Obst. & Gynec. Brit. Emp. **64**: 361, 1957.
18. Martinez, S. A. and Mantilla, M. J. M.: Acta. Gynec. (Madr). **10**: 213, 1959.
19. Mullick, S., Bagga, O. P. and Mullick, V. D.: Am. J. Obst. & Gynec. **89**: 767, 1964.
20. Oliver, M. F. and Boyd, G. S.: Clin. Sc. **14**: 15, 1955.
21. Owen, C. A. Jr. and McKenzie, B. F.: J. Appl. Physiology. **6**: 696, 1954.
23. Scandrett, F. J.: In Modern Trends in Human Reproductive Physiology. Edited by Carey, H. M. London 1963, Butterworths & Co., p. 215.
24. Spaet, T. H. and Kinsell, B. G.: Proc. Soc. Exptl. Biol. Med. **84**: 314, 1953.
25. Stamm, H.: Koagulopathien, IVth Hamburger Symposium, uber Blutgerinnung. Stuttgart, F. K. Scharrauer Verlag, 1962.
26. Von Studnitz, W.: Scandinav. J. Clin. Lab. Invest. **7**: 324, 1955.