MATERNAL SERUM HEAT STABLE ALKALINE PHOSPHATASE LEVEL AS A DIAGNOSTIC PARAMETER FOR FOETAL MATURITY AND PLACENTAL FUNCTION

by

K. SUNANDABAI,* M.D., D.G.O.,

PRATIBHA ROHATGI,** M.S., D.G.O.,

MEERA AGNIHOTRI,*** M.S., D.G.O.

and

B. LAHIRI,**** M.D., M.R.C. Path.

Accurate assessment of foetal maturity and placental function becomes essential for the management of certain cases where termination of pregnancy at a certain period of gestation is indicated in the interest of foetus, mother or both. A sensitive and precise parameter of both must be known, otherwise a foetus who escapes foetal dysmaturity or intrauterine death will die of prematurity after birth.

Increased levels of maternal serum alkaline phosphatase in late pregnancy have been described by various workers (Coryn, 1934; Meranz *et al*, 1937; Young *et al*, 1946; Beck and Clark, 1950; Freidman & Lapan 1961; Zuckerman *et al* 1965; Peter and Parihar 1968; Gupta *et al*, 1969). Total alkaline phosphatase found in maternal serum is of two origins, placental and non-placental. A simple method to differentiate between human serum alkaline phosphatase of placental and non-placental origin was described by Mcmaster *et al*, (1964) and Neale *et al*, (1965). These authors also reported that the alkaline phosphate of placental origin is heat stable and rises progressively with advancing gestation, while non-placental alkaline phosphatase remains within normal limits throughout pregnancy and is heat labile The present study was undertaken to study the maternal serum alkaline phosphatase levels with special reference to heat stable fraction in relation to maturity and placental function.

*Prof. & Head of the Deptt. of Obstetrics & Gynaecology.

**Reader in Obstetrics & Gynaecology.

***Resident Gynaecological Officer.

****Professor of Pathology, G.S.V.M. Medical College, Kanpur.

Received for publication on 19-12-1972.

Material and Methods

Cases for the present study were selected from the antenatal clinic and in-patient section of Upper India Sugar Exchange Maternity Hospital, Kanpur. Serum alkaline phosphatase was estimated in 25 normal non-pregnant women of child bearing age (control group) and 185 cases of pregnancy in whom estimations were done during different weeks of pregnancy extending from 28 to 42 weeks.

The alkaline phosphatase was estimated by Powell and Smith modification of King and King method.

A total of 210 cases were studied which were divided into 2 groups.

1st group (control Group)

Comprised of 25 cases where serum alkaline phosphatase levels were estimated

TABLE I

Different Fractions of Serum Alkaline Phosphatase Levels in Normal Non-pregnant Women of Child Bearing Age

Abreviations	No. of cases	Total serum alkaline phosphatase level	Heat stable alkaline phosphatase level	Heat labile alkaline phosphatase	% of heat stable with TSAP level
		T.S.A.P.	H.S.A.P.	H.L.A.P.	HS with TSAP
Range	25	3.60-13.00	0.10-1.33	2.3-12.6	2-28
Mean		2.87	0.68	7.19	—
Standard deviation		±2.93	±0.32	±2.93	—

TABLE II

Different Fractions of Alkaline Phosphatase Levels in K.A. Units/100 in Cases of Pregnancy

No. of cases	Duration of pregnancy (weeks)	Total serum alkaline phosphatase			Heat stable alkaline phosphatase			Heat labile alkaline phosphatase			Percentage of (ii) to (i)
		Range	Mean	Standard deviation	Range	Mean	Standard deviation	Range	Mean	Standard deviation	
15	28-29	7.60-11.90	9.19	1.12	0.40- 4.50	1.61	1.11	5.00-10.20	7.57	1.15	3.72-37.82
20	30-32	9.20-15.30	11.91	1.51	3.20- 7.90	5.14	1.57	4.30- 8.80	6.76	1.21	25.21-60.32
10	33-34	12.00-16.50	14.41	1.02	6.90- 9.20	8.03	0.80	4.40- 7.50	6.38	1.09	48.28-66.67
10	35 weeks	12.90-18.90	14.70	1.64	6.80-11.50	8.29	1.41	4.33- 7.60	6.41	0.98	48.28-66.43
20	36 weeks	13.90-18.0	15.45	1.30	6.90-10.70	8.84	1.06	4.20- 8.30	6.60	1.17	49.64-70.42
20	37 weeks	14.0 -18.6	16.45	1.02	7.20-12.20	9.80	1.08	4.40- 8.00	6.65	0.91	48.65-73.49
30	38 weeks	14.9 -20.6	16.82	1.35	7.60-12.30	10.1	1.17	4.40- 8.40	6.71	0.82	51.01-73.49
30	39 weeks	16.20-20.1	18.34	1.15	9.30-13.10	11.48	0.95	9.40-98.00	6.86	1.18	48.69-74.27
55	40 weeks	16.90-24.4	19.13	1.21	10.60-15.90	12.46	0.95	4.10-11.20	6.67	1.00	54.10-74.30
19	41 weeks	16.0 -22.0	19.12	1.55	9.70-14.60	12.71	1.23	5.20- 7.70	6.41	0.81	60.63-72.49
10	Post-maturity	20.0 -24.9	22.74	1.45	13.0 -19.8	15.41	1.74	5.10- 8.70	7.33	1.17	60.75-79.52

in normal non-pregnant women of child bearing age.

2nd group (study group)

Comprised of 185 cases in which serum alkaline phosphatase levels were estimated during different weeks of pregnancy extending from 28 weeks to 42 weeks, including postmaturity and cases of unknown duration of pregnancy. Single as well as multiple follow-up studies were performed on individual cases.

Observations

Table 1 shows different fractions of serum alkaline phosphatase levels in normal non-pregnant women of childbearing age in K.A. units/100 c.c.

Table II shows values of different fractions of alkaline phosphatase levels in K.A. units/100 ml. of serum in cases of pregnancy in different weeks of gestation and Table III shows the values in cases of pregnancy where the duration of pregnancy was doubtful.

Discussion

In spite of marked individual variation in the total serum alkaline phosphatase levels (3.6 to 13 K.A. units) in cases of normal non-pregnant females of child bearing age, there is one significant feature that the heat labile alkaline phosphatase contributes to most of the total serum alkaline phosphatase, the heat stable fraction being very small. Similar findings have been reported by Peter and Parihar (1968); Lee and Lewis (1963) and Meranze and Meranze (1937).

In cases of pregnancy, rise of H.S.A.P. was noticed throughout the pregnancy The pattern of rise was variable in the 1st and 2nd trimesters and was not significant, but in the 3rd trimester the rise was well marked having a definite pattern. There was a steady and gradual rise by 0.5 to 1.5 K.A. units/100 ml./week from the 35th week upto 40 weeks. It remained constant or showed a very slow insignificant rise from

TABLE III

Total and Heat Stable Serum Alkaline Phosphatase in Cases of Unknown Duration of Pregnancy in K.A./100 ml.

Sl. No.	Case No.	Duration of gestation in question	Total serum Alkaline phosphatase	Heat stable Alkaline Phosphatase	Calculated duration of gestation
1	55	? Full term	14.80	10.10	36 weeks
2	57	? Full term	16.00	9.0	37 weeks
3	58	? Post Mature	17.00	10.0	37 weeks
4	88	? Full term	16.80	10.0	39 weeks
5	89	? 43 weeks	18.50	10.6	39 weeks
6	103	? Post Mature	17.00	10.1	Full Term
7	108	? 38 weeks	23.40	16.0	Post Mature
8	111	? 37 weeks	21.40	14.40	40 weeks
9	119	? Full Term	17.90	12.0	39 weeks
10	129	? Full Term	17.90	11.60	38 weeks
11	136	? 44 weeks	16.50	11.00	37 weeks
12	147	? 40 weeks	15.2	9.0	Full Term
13	155	? Post Mature	19.70	12.30	Full Term
14	159	? Post Mature	18.60	11.60	Full Term
15	167	? Full Term	19.50	11.90	41 weeks
16	168	? Post Mature	11.50	11.0	38 weeks

40 weeks to 41 weeks, and after that it showed a rise again at 42 weeks. Peter and Parihar (1968) did not notice any rise after 40 weeks. Curzen and Morris (1966) have reported a gradual rise of H.S.A.P. levels from 28th to 38th week, then a decrease upto 41 weeks, rising again to reach the peak value at 42 weeks. Bagga *et al,* (1969) have noticed maximum rise upto 36 weeks.

T.S.A.P. between 15-20 K.A. units/100 ml and H.S.A.P. between 10-12 K.A. unit/100 ml. indicate a term pregnancy. If H.S.A.P. at term is 15 K.A. unit/100 ml. or more a close follow up of the case should be done so that any pathological fluctuation in the scheduled curve may be detected at the earliest for placental insufficiency. Another important finding was that in spite of the marked individual variation in H.S.A.P., the mean value rises gradually and H.S.A.P. constitutes 50% or more of the T.S.A.P. This finding is in close agreement with those of Peter and Parihar (1968) and Gupta *et al.* (1969). Placental sufficiency or insufficiency is detected by any alteration in the normal gradually rising curve of H.S.A.P. on serial study. H.S.A.P. levels of 5 K.A. units/100 ml or less after 38 weeks is a sign of placental insufficiency. In three cases who were admitted during labour, H.S.A.P. levels were found to be 4.4, 4.5 and 5.K.A. units/100 c.c. All the babies had peripheral cyanosis at birth. Two of them expired on the 1st and 3rd day while the 3rd baby could be revived with difficulty. In one of the cases in whom serial estimations of H.S.A.P. was done at 36, 41 and 42 weeks, values of 10.7, 13.0 and 4.4 K.A./100 ml were detected. Because of the sudden fall at 42nd week the patient was advised immediate termination of pregnancy to which she did not agree. After 4 days she was admitted in labour. The baby could be revived with difficulty but expired six hours later. In this case the death of the foetus was obviously due to postmaturity resulting in placental insufficiency which was avoidable. In two cases in this series, maternal H.S.A.P. values were found to be 19.6 and 19.0 K.A. units 100 ml. (more than what was expected at term). In both the cases the babies were found to be dysmature with yellow discolouration of cord and nails. In 49 cases more than one study of serum alkaline phosphatase was done during different gestation ages. In a few cases more than five serial estimations were performed during different weeks of gestation. In all the normal cases the serum alkaline phosphatase level showed a constant pattern of a gradual rise of heat stable fraction with a corresponding rise in total alkaline phosphatase with advancing gestation. But findings of one case if compared with the other in the same gestation week showed marked variation perhaps due to individual variation in placental activity.

References

1. Bagga, O. P., Mullick, U. D. and Maclan, P.: Am. J. Obst. & Gynec. Brit. Cwlth. **71: 397, 1965.**
2. Beck, E. and Clark, L. C.: Am. J. Obst. & Gynec. **60: 731, 1950.**
3. Coryn, G. (1934): quoted by Mc Master et al: Jour. of Obst. & Gynec. Brit. Cwlth. **71: 735, 1964.**
4. Curzen, P. and Morris, I.: J. of Obst. & Gynec. Brit. Cwlth. **73: 64, 1966.**
5. Friedman, M. and Lapan, B.: Amer. J. Obst. & Gynec. **82: 132, 1961.**
6. Gupta, U., Gupta, A. K. and Mittal, V. K.: J. Obst. & Gynec. Ind. **21: 700, 1969.**
7. Lee, A. B. H. and Kewus, P. L.: Amer. J. of Obst. & Gynec. **87: 1071, 1963.**
8. McMaster, Y., Tennant, R., Clubb,

J. S. and Neale, F. E.: J. Obst. & Gynec. Brit. Cwlth. **71**: 737, 1964.
9. Meranze, T., Meranze, D. R. and Rothman, M. M.: Amer. J. Obst. & Gynec. **33**: 444, 1937.
10. Neale, F. C., Clubb, J. S., Hotchkis, D. and Posen, S.: Jour. Clin. Path. **18**: 359, 1965.
11. Peter, E. and Parihar, T.: J. Obst. & Gynec. India. **18**: 9, 1968.
12. Young, J., King, E. J., Wood, E. and Wootton, I. D. P.: J. Obst. & Gynec. Brit. Empire. **53**: 251, 1946.
13. Zuckerman, H., Saovsky, E. and Kellner, B.: Obst. & Gynec. **25**: 819, 1965.