COMPARATIVE STUDY OF URINARY OESTRIOL AND SERUM HEAT STABLE ALKALINE PHOSPHATASE AS A GUIDE TO PLACENTAL FUNCTION

by

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Diagnosis of placental efficiency and insufficiency is difficult and still a subject of discussion. Although there are many means to guess its efficiency, there is need for a more accurate and reliable method.

Increased levels of maternal urinary oestrogen (Diczfalusy, 1957; Diczfalusy and Lauritzen, 1969; Klopper and Billewiez, 1963) and serum heat stable alkaline phosphatase (Peter and Parihar, 1968) in late pregnancy have been described.

The oestriol levels in the maternal urine directly reflect the functioning of the feto-placental unit. Total stable alkaline phosphate present in the maternal serum is of two origins—placental and non-placental. McMaster *et al* (1964) described the unique property of heat stability of the placental alkaline phosphatase.

The present study has been conducted to compare the usefulness of 24 hours urinary oestriol excretion and serum heat stable alkaline phosphatase levels in detecting placental efficiency.

Material and Methods

Cases were selected from antenatal clinic and the Ward of S.S. Hospital attached to the Institute of Medical Sciences, Varanasi.

TABLE I
Distribution of Cases

Group	Condition	No. of cases	No. of paired observations
i	Normal pregnancy	25	148
ii	Toxaemia	22	80
iii	Intra-uterine growth retardation	15	72
iv	Antepartum haemorrhage	10	22
v	Twins	4	18
vi	Diabetes	1	6
vii	Unexplained fetal loss in previous pregnancy	5	24
	Total	82	370

The type of cases contributing the material are shown in Table I. Complete 24 hours urine samples were collected without preservative. The blood was obtained by vein puncture.

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Urinary oestriol was assayed by Cohen's modification of Kober-Brown-Nock procedure. Heat stable alkaline phosphatase was determined according to King and Armstrong method modified by King (1951), after heating the serum at 65°C for 30 minutes in a water bath. A total of 82 cases were studied between 28 to 40 weeks of gestation yielding 370 paired estimation of urinary oestriol and serum H.S.A.P.

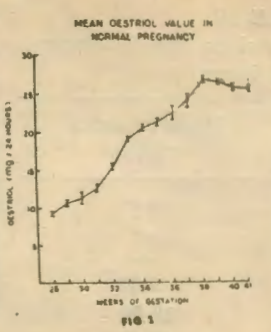
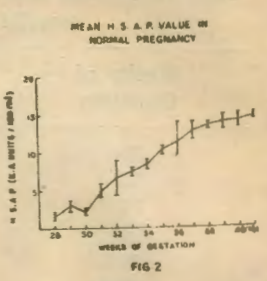


Fig. 1
Mean Urinary oestrial in normal pregnancy.



Fg. 2
Mean serum H.S.A.P. in normal pregnancy.

Observations

Normal Pregnancy: In normal pregnancy both—mean oestriol and mean serum H.S.A.P. showed gradual rise with the advancement of pregnancy, as shown in Figs. 1 and 2 and Tables IV and V. Twenty-five babies from these pregnancies were studied in relation to birth weight and pre-confinement level of urinary oestriol and serum H.S.A.P. Urinary oestriol was very closely related to the fetal birth weight ($r = 0.9018, P < 0.001$) as shown in Table II. There was no significant relationship between serum H.S.A.P. and fetal weight ($r = 0.2539$, $P > 0.10$). Correlation of weight of each of placenta with oestriol and H.S.A.P. values before confinement has been shown in Table III. There was a close relationship between crude placental weight and urinary oestriol ($r = 0.9536, P < 0.001$). There was no significant relationship between H.S.A.P. and placental weight ($r = 0.0056$, $P > 0.10$).

TABLE II

Weight of Baby in Relation to Oestriol Excretion H.S.A.P. Levels Before Confinement (Normal Pregnancy)

Weight of baby (lbs)	No. of cases	Mean oestriol excretion (mg./24 hours)	Mean H.S.A.P. (KA unit/100 ml.)
5-6	9	21.13	12.11
6-7	9	27.87	12.11
7-8	4	28.10	15.00
8 and above	3	31.43	11.23

TABLE III

Weight of Placenta in Relation to Oestriol Excretion and H.S.A.P. Level Before Confinement (Normal Pregnancy)

Weight of the placenta (lbs)	Number of cases	Mean oestriol values (mg/24 hrs.)	Mean H.S.A.P. values (KA unit/100 ml.)
½ 1	1	16.00	12.00
< 1	7	21.95	12.00
— 1	17	28.53	11.35

TABLE IV
Normal Urinary Oestriol in 3rd Trimester (mg./24 hours)

Weeks of Gestation	Present series (1975)
25	—
26	—
27	—
28	9.18
29	10.50
30	11.23
31	12.59
32	15.33
33	19.03
34	29.33
35	21.10
36	22.10
37	24.10
38	25.74
39	24.56
40	24.67

TABLE V
Normal Serum H.S.A.P. in 3rd Trimester (KA units/100 ml.)

Weeks of Gestation	Present series
28	1.61
29	3.16
30	2.25
31	5.14
32	6.75
33	7.57
34	8.29
35	9.80
36	10.53
37	11.91
38	12.46
39	12.71
40	14.41
41	14.07

Pregnancy with Toxaemia: There is a gradual rise in the urinary oestriol till 37th to 38th weeks in mild and till 36th week in severe cases of toxaemia and then there is a fall in the output. On the contrary H.S.A.P. rose till term and it was abnormally high in cases of severe toxaemia. Mean value of oestriol in these cases was lower than the normal mean value for the corresponding period of gestation. Mean value of H.S.A.P. do not show any significant rise or lowering from the normal mean values for the corresponding period of gestation. H.S.A.P. in severe cases of pre-eclamptic toxaemia showed a higher value compared to the normal mean. In essential hypertension H.S.A.P. was within normal level but oestriol was on the lower side.

Pregnancy with Intrauterine Growth Retardation: The mean difference in oestriol level between this group of cases and normal pregnancy was 3.29 at 32 weeks of gestation which rose to 7.39 at 38 weeks. The 't' values from 32-36 weeks was 4.21 ($P < 0.001$) the 't' values at 38 weeks was 5.83 (P 0.001). This signified that values are low and statistically significant in intrauterine growth retardation. No such correlation was found in H.S.A.P. in normal and intrauterine growth retardation.

Pregnancy with Antepartum Haemorrhage: Urinary oestriol values showed a progressive rise and serum H.S.A.P. also showed gradual rise with the advancement of gestation.

Twin Pregnancy: Both the urinary oestriol estimation and serum H.S.A.P. are higher than that obtained in single pregnancy. There is a gradual rise in the excretion of oestriol from 28 weeks onwards till 36 weeks at which period highest mean value of 24.38 mg/24 hours was obtained. In contrast the values of serum H.S.A.P. were always above the upper limit of normal so that at 40 weeks the mean H.S.A.P. level was 24.40 KA units/100 ml. Placenta of these cases weighed more than 2 lbs.

Pregnancy with Diabetes: No particular conclusion could be drawn from only 1 case included in this study.

Unexplained Fetal Loss in Previous Pregnancy: Patients who have lost one or more babies in the previous pregnancies were studied. The oestriol level was on the lower side compared to normal pregnancy for similar gestation. Mean H.S.A.P. value did not show any alteration.

Discussion

The fetus in uterus is comparatively inaccessible. Various methods of assessing the fetal wellbeing are therefore dependant upon the assessment of placental well being. Fetus and placenta have been recognised as equal partners in feto-placental unit (Diczafalusy and Lauritzen, 1961). The measurement of function in one part of the unit automatically measures the function of the other.

In the present work a comparative study of urinary oestriol and serum H.S.A.P. has been done to know which one is more sensitive and accurate out of the two H.S.A.P. originates almost from the trophopblast of the placenta and might therefore be more indicative of true placental function. Serum oestriol essay pattern has shown wide scatter of values, urinary oestriol essay having been recognised as more accurate.

In normal pregnancy there is considerable rise in placental production of both oestrogen and H.S.A.P. Of wider scatters of oestriol values the lower limit from 28 to 30 weeks was 6 mg. From 31 to 35 weeks, no value fell below 10 mg. From 31 to 40 weeks the values did not fall below 16 mg. Usually the values remained above 20 mg. in 24 hours. Similarly inspite of wide scatters of value of serum H.S.A.P. levels the lower limit from 28 to 30 weeks was 1.04 KA unit. From 31 to 35 weeks the values did not fall below 7 K.A. unit.

In patients with severe degree of toxaemia the urinary oestriol was 8.02 mg at 38 weeks in contrast to 9.10 mg at 32 weeks gestation suggesting premature ageing of the placenta in these cases.

Mean H.S.A.P. level was abnormally high being 10.00 KA units at 32 weeks and 25.03 KA units at 38 weeks. This elevation may be due to placental tissue damage or ageing. Curzen and Morris (1966-68) and Hunter (1969) found high values in severe pre-eclampsia.

Nearly all authors on this subject are agreed that when the fetal growth is retarded there is a tendency for oestriol output to be low. Abrupt fall or rise in H.S.A.P. has been reported (Messer, 1967; Hunter, 1969; and Quigley *et al*, 1970) as an ominous sign of falling placental function. In our opinion, for monitoring small for dates fetuses urinary oestriol seems to be a better guide than H.S.A.P. as suggested by Watney *et al* (1970), Pertrucco *et al* (1973).

The oestriol values in antepartum haemorrhage fell within the accepted range of normal. Mean H.S.A.P. is slightly higher than normal mean but within the acceptable range of normal.

The oestriol values at 35-36 weeks were high in twin pregnancy as compared to singleton pregnancy and correspond to the values that are encountered 2-3 weeks postdated normal pregnancy. This is in conformity with Brown and Veall (1953) that twins are post mature at 40 weeks. Coyle and Brown (1963) found higher oestriol values in twin pregnancies but were comparable to the values in singleton pregnancies with babies weighing more than 8 lbs.

Abnormally high H.S.A.P. levels have been found in the present series, the

highest mean values being 21.40 KA unit at 40 weeks as compared to 13.56 KA unit/100 ml. in the singleton pregnancy. This is quite similar to the study of Peter and Parihar (1968), McMaster *et al* (1964), and by many other workers. The higher values in the present study may be due to large size of the placenta as in all 4 cases placenta weighed more than 2 lbs.

All 5 cases included under unexplained foetal loss in previous pregnancies had 1 or more unexplained fetal death during previous pregnancies. In 1 case oestriol excretion of 12.46 mg. at 35-36 weeks fell to 10.20 at 37 weeks suggesting placental dysfunction and pregnancy was terminated. Other 4 cases had their oestriol excretion and H.S.A.P. level within normal limit and had spontaneous vaginal deliveries with live babies.

Present work concludes that urinary oestriol estimation is a better index than serum H.S.A.P. for evaluation of placental efficiency.

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