URINARY OESTROGEN LEVELS AS AN INDEX OF FOETAL WELLBEING

by

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Introduction

Out of the several tests available so far the estimation of urinary oestriol levels is a fairly reliable method of judging the foeto-maternal status during the later weeks of pregnancy.

The usefulness of oestriol estimations has been proved from time to time in the management of pregnancies complicated by toxaemia, diabetes and intrauterine growth retardation of the foetus, especially for timing the delivery of the foetus in best possible condition. The present study was undertaken to assess the utility and practicability of this estimation as an index of foetal wellbeing.

Material and Methods

One hundred and ten patients were studied from those attending the antenatal clinic in the Sassoon General Hospital, Poona, during the period of 14 months from January, 1973 to February, 1974. Only those patients who were in the second half of pregnancy were selected for the study. After admission the patients were given explicit instructions regarding the collection of the 24 hours urine sample. The sample was collected the next morning and was analysed for its oestrogen content by using the method of Montague (1964). This technique measures the total oestrogen rather than oestriol.

Since in late pregnancy over 90% of the oestrogen is in the form of oestriol, estimation of total oestrogens excreted was taken as a good measure of the oestriol excretion. This method was particularly chosen for the study as it is simple, easy and can be carried out on a small quantity, 1-5 ml. of urine. The distribution of the 110 cases studied is shown in Table I.

TABLE I
Distribution of Cases

Type of case	No. of cases
Normal pregnancy	62
Mild toxaemia	12
Severe toxaemia	13
Intrauterine growth retardation of the foetus	7
Twin pregnancy	8
Intrauterine death of foetus	4
Prolonged pregnancy	2
Pregnancy complicated by diabetes	2
Total	110

Observation and Results

(A) *Normal Pregnancy:* A total of 81 estimations were carried out on 62

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pregnant women at different periods of gestation in the second half of pregnancy. All these cases had normal past obstetric history and no complication in the present pregnancy.

Table II shows the results obtained in this group of cases. It appears from Table II that even in normal pregnancy there is a wide range of variation in the oestriol excretion at a given period of gestation. Moreover, there is a progressive rise in the urinary oestrogen levels from 24 weeks till term, after which a slight fall is observed. There appears to be a significant correlation between the gestational period in weeks and the oestrogen value in mg per 24 hours. ($r = 0.6505$).

The urinary oestrogen levels in the last few weeks of normal pregnancies and the birthweight of the babies in these cases were statistically analysed. Table III shows the correlation of the oestrogen levels with the weight of the newborn. It was found that there is a significant correlation between the urinary oestrogen levels and the birthweight ($r = 0.4152$).

(B) *Complicated Pregnancies:* Urinary oestrogen levels in 42 normal cases between the 36th-40th week of gestation were compared with those in 29 cases of complicated pregnancies of the comparable period of gestation.

The results are shown in Table IV. On statistical analysis it was found that:

(a) In cases of mild as well as severe toxaemia the urinary oestrogen levels were significantly lower than those in normal pregnancy. ($P < 0.00001$).

(b) In pregnancies complicated by intrauterine growth retardation of the foetus the urinary oestrogen levels were significantly lower ($P < 0.00001$) and the

TABLE II
Urinary Oestrogen Levels in Normal Pregnancy

Duration of pregnancy in weeks	No. of estimations	Range of oestrogen in mg/24 hrs.	Mean in mg/24 hrs.	S.D.
24	2	6.4-10	8.20	2.545
26	4	10.0-14.7	11.45	2.182
28	9	8.3-17.0	13.067	3.148
30	8	11.2-22.0	17.175	3.793
32	10	11.5-22.6	20.31	5.291
34	6	18.7-30.0	22.70	4.248
36	19	14.3-42.0	27.00	8.773
38	13	13.5-47.6	28.90	10.718
40	10	17.0-40.0	26.8	8.321

TABLE III
Correlation of Oestrogen Levels With Weight of the Newborn

Weight in gms.	1000	1500	2000	2500	3000	3500
No. of patients	2	6	7	22	17	9
Oestrogen value in mg/24 hrs.	9.5	16.89	19.23	27.42	32.55	32.83

TABLE IV

Comparative Study of Urinary Oestrogen Levels in Normal and in Complicated Pregnancies (Period of gestation—36 to 40 weeks)

Type of case	No. of estimations	Range of values in mg/24 hrs.	Mean in mg/24 hrs.	S.D.
Normal pregnancy	42	13.5-47.6	25.576	9.136
Mild toxaemia	10	11.0-35.7	22.46	9.182
Severe toxaemia	7	10.0-22.3	14.73	4.12
IUGR of the foetus	12	5.4-17.9	11.56	3.979
Twin pregnancy	8	21.0-55.0	33.11	10.065

values failed to rise from week to week thus showing a typical flat curve as illustrated in Fig 1.

The cases having pregnancies complicated by diabetes mellitus, intrauterine death of the foetus, prolonged period of gestation (> 42 weeks) and twin pregnancy being few in number were considered together in the miscellaneous group. Table V shows the oestrogen levels in this group. In 4 cases of intrauterine death of the foetus the range of values was from 3-3.5 mg/24 hour.

Of the 2 cases of prolonged pregnancy, 1 had the oestrogen levels of 11.7 mg in the 43rd week and labour was induced on the same day. The patient had a normal delivery with a baby weighing 3000 gms. Two pregnancies were complicated by diabetes. One case had mild and controlled diabetes and the oestrogen level was normal. The second case had severe juvenile diabetes. Her oestrogen levels were estimated serially from the 26th week onwards. The graph was plotted

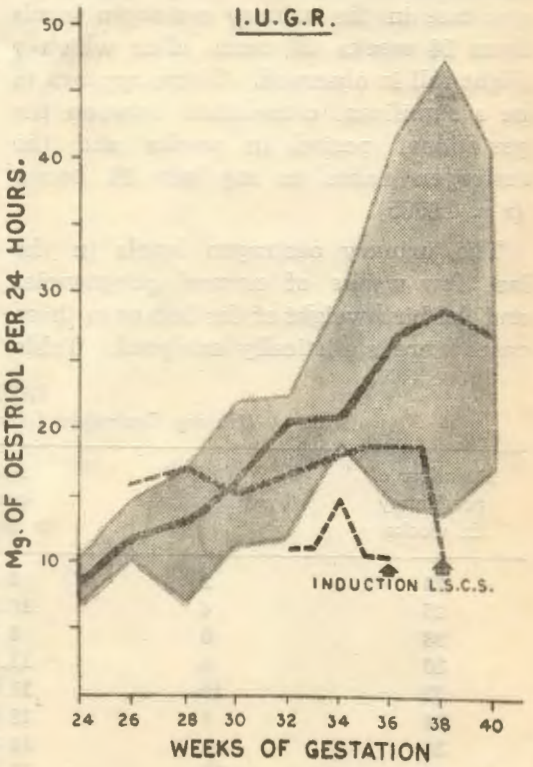

Fig. 1

TABLE V

Urinary Oestrogen Levels in Miscellaneous Cases

Type of case	No. of cases	Period of gestation	Range of value in mg/24 hrs.
Intrauterine death of the foetus	4	30-32 wks.	3.0- 3.5
Prolonged pregnancy	2	42-43 wks.	11.7-27.0
Diabetes	2	37-40 wks.	11.0-21.0
Twin pregnancies	8	37-40 wks.	21.0-55.0

and the curve was seen to be horizontal and below the average curve, which suggested retarded growth of the foetus.

Elective caesarean section was done in the 39th week and the baby weighed 2200 gms. All 8 cases of twin pregnancy showed a significantly higher urinary oestrogen levels. ($P < 0.00001$). These high values could be due to the double supply of precursor substances from two foetal adrenals.

Discussion

Present study reveals that there is progressive rise in the urinary oestrogen levels as pregnancy advances. This finding is in agreement with the findings of Macleod *et al* (1975), Dhall and Wakhaloo (1967), Ganguli *et al* (1973) and several others the values obtained in present study seem to be higher than those reported by Shahani and Merchant (1977), Krishna, *et al* (1973) which could be attributed to the different method adopted in our laboratory for the estimations. However, the values in the present study are quite in agreement with those of Jenkins *et al* (1977), Klopper *et al* (1963) and Ganguli *et al* (1973). Since the mean excretion figures obtained by different workers do not give any idea regarding the true status of the functioning of the foeto-placental unit, and since the serial estimations and the relation of the values to the previous values are indicative (vide infra) the difference in the mean values does not matter much.

A significant correlation was noted in normal pregnancy between urinary oestrogen levels and the weight of the newborn. Similar observations have been made by Shahani and Merchant (1977), Dhar and Rashid (1977) and Beling (1967).

Urinary oestrogen estimation promises to be a valuable aid to the Obstetrician particularly in the 'high risk pregnancies', where the placental degenerative changes set in quite early jeopardising the foetal wellbeing. This leads to the retardation of the growth of the foetus and even to intrauterine death of the foetus without any clinical signs indicating the impending danger to the foetus. Since the placental syncytium is the site of synthesis of oestrogens from the foetal and maternal precursors during pregnancy, placental degenerative changes will be reflected in the decreased urinary oestrogen levels which can therefore be a very useful guide to the obstetrician in timing the delivery of the foetus. Thus, a falling value in pregnancies complicated by pre-eclamsia, diabetes mellitus or in other placental insufficiancy conditions is indicative of impending danger to the foetus. Significantly low values observed in present study in such conditions are in agreement with the findings of Banerjee (1962), Beling (1967), Dhall and Wakhaloo (1967), Macleod *et al* (1971) and Dhar and Rashid (1977).

Sudden drop in the oestrogen values following initial normal levels suggests intrauterine foetal jeopardy. Outcome of 2 such cases has been shown in Fig. 2, where sudden fall in levels was associated with premature delivery of stillborn babies. As in both these cases babies were too premature at the time of such fall, nothing could be done to save them, but if such a fall were observed in later weeks of pregnancy, it would have been possible to induce labour in the interest of the baby. Such a decision can be taken only when the estimations are carried out serially from the onset of third trimester of pregnancy.

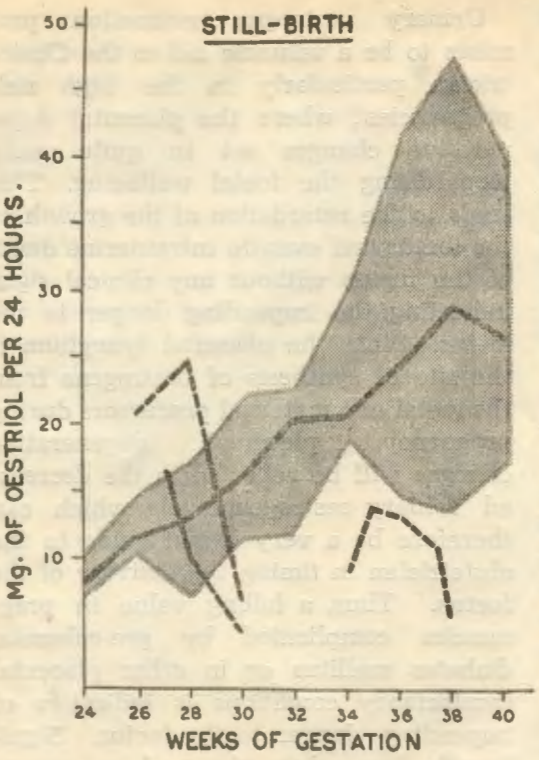

Fig. 2

Beling (1967) has shown that three falls in the oestriol values are associated with intrauterine death of the foetus. Hence, after the 34th week it seems justifiable to terminate the pregnancy if 2 falling values are reported from the laboratory on 2 consecutive days. Though in majority of cases the low oestrogen levels are associated with the diminution of the function of foeto-placental unit, it is not uncommon to see cases with low oestrogen levels terminating in a good outcome and thus a sudden drop in the serially estimated levels is of more significance than a single low value as such.

However the routine use of this estimation has got certain drawbacks, the main being that the procedure is time consuming and the estimations require a 24 hour urine collection. Therefore, the results when received by the clinician indicate the foetal status at least 24 hours prior to the time of estimation. Moreover, a 24 hour urine collection is rather inconvinient and could sometimes be incomplete, which then would affect the overall accuracy of the results.

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