

COMPARISON OF SERUM COPPER AND URINARY OESTRIOL IN THE ASSESSMENT OF PLACENTAL FUNCTION IN HIGH RISK PREGNANCY

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The early diagnosis of failing placental function and of foetal jeopardy is one of the most important difficult problems of obstetric practice today. Clinical assessment of placental function and of foetal well-being is not always accurate as is clearly indicated by a number of foetuses that still die in utero. So a practical and reliable test for placental function would be of great value in our efforts to reduce further stillbirth and perinatal mortality.

Serial oestriol assays have been used to assess foeto-placental function in high-risk pregnancy (Frandsen and Stake-mann, 1960; Ten Berg, 1960; Greene and Touchstone, 1963; Klopper, 1968). O'Leary (1969) observed marked fall in serum copper level prior to foetal death in toxæmia of pregnancy. He therefore, suggested that estimation of serum copper in pregnancy might be useful in the assessment of placental function and foetal well-being.

Copper is significantly elevated in pregnant women. The increase in its level is quite obvious as early as in first two months of gestation, but the values are near the maximal level found in women

who are not pregnant. With the end of first trimester however, and particularly with the beginning of fourth month of pregnancy serum copper rises rapidly and abruptly reaches high values. Thereafter, serum copper continues to increase progressively and gradually as pregnancy advances and it reaches its highest level in ninth month of pregnancy followed by a decrease just before the delivery.

The present analysis has been done to assess the comparative value of both the tests i.e. 24 hours' oestriol excretion and serum copper level to assess the foeto-placental dysfunction.

Material and Methods

The present work was carried out in the Department of Obstetrics and Gynaecology, Patna Medical College Hospital. Cases were selected randomly from the patients attending Out-patients' Department, antenatal clinic, labour room and indoor wards. Only those cases were included in this study who had pregnancy of 37 weeks or more. The duration of gestation was calculated from the date of last menstrual period. The patients were of different age group, parity and social classes. Detailed history was taken and thorough clinical examination was done in each case. Besides routine investiga-

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tions, estimation of oestriol in 24 hours sample of urine was done in Departmental Laboratory by the method of Oakay (1967). Estimation of serum copper was done by the atomic absorption spectrophotometer in the Department of Geology, Patna University, and mode of delivery, condition of baby at birth and birth weight were also recorded.

and serum copper was done in 80 cases of high-risk pregnancy and 20 cases of normal pregnancy. The aim was to make a comparative analysis of urinary oestriol output and serum copper level in the assessment of placental function. In the cases selected for study, duration of gestation varied from 37 to 40 weeks except in cases of postdate pregnancies in which the

TABLE I

Urinary Oestriol Value in 24 Hours Urine and Serum Copper in 20 Cases of Normal Pregnancy at 37 to 40 Weeks of Gestation

Duration of pregnancy in weeks	No. of cases	Urinary oestriol in mgm/24 hours			Serum copper in microgram per dl		
		Range	Mean	S.D.	Range	Mean	S.D.
37-40	20	17.1-31	22.37	3.87	194-248	220.1	15.35
't'	54.43	'r'	-.89

Mean urinary oestriol level in 20 cases of normal pregnancy at 37 to 40 weeks gestation was 22.37 mgm/24 hours, whereas the mean serum copper level was 220.1 microgram/dl. When statistically calculated there was no correlation between serum copper and urinary oestriol values in normal pregnant at term ('r' being $-.89$).

Discussion

Present study includes 100 cases, 20 cases with normal pregnancy and 80 cases with high-risk pregnancy between 37 to 42 weeks gestation. Estimation of urinary oestriol was done on 2 to 3 consecutive days in most of the cases and the mean value was obtained in each case. This was done to minimize day-to-day variability in oestriol excretion. As stated by Fuchs and Klopper (1977) daily fluctuations in oestriol excretion can be as much as $\pm 40\%$, therefore, at least 3 values are necessary to establish a trend. Estimation of copper was done once in each case.

Estimation of 24 hours urinary oestriol

duration of gestation varied from 41 to 42 weeks (Table I). Mean urinary oestriol in normal pregnant women was found to be 22.37 ± 3.87 mgm/24 hours (range being 17.1 to 31 mgm/24 hours), whereas mean serum copper level was 220.1 ± 15.35 microgram/dl (range was 194 to 242 microgram/dl). No statistical correlation between urinary oestriol serum copper level in normal pregnancy was observed ($r = -.89$). Age, parity, socio-economic status of the mother and sex of the baby were not found to influence either the urinary oestriol output or the serum copper level. Urinary oestriol level was found to correlate with the birth weight of the baby, whereas serum copper level failed to correlate with birth weight (Table II). Mean urinary oestriol in patients who delivered growth retarded babies was 9.49 ± 3.06 mgm/24 hours which was significantly lower than the mean value obtained in normal pregnancy ($p < 0.01$). Mean serum copper level in intrauterine growth retardation (219.6 ± 15.14 microgram/dl) was, however,

TABLE II
 Urinary Oestriol in mgm/24 Hours and Serum Copper in Microgram/dl in Normal Pregnancy and High-risk Pregnancy

Types of cases	No. of cases	Duration of gestation in week	Urinary oestriol in mgm/24 hours			Serum copper in microgram/dl			't' value	'p' value
			Range	Mean	S. D.	Range	Mean	S. D.		
Normal	20	37-40	17.1-31.0	22.37	3.87	194-242	220.1	15.35	—	—
I. U. G. R.	9	37-40	6.5-15.6	9.49	3.06	195-242	219.6	15.14	0.07	>0.05 not significant
Mild toxæmia	20	37-40	7.0-25.5	17.50	5.02	194-246	222.9	15.03	0.57	>0.05 not significant
Severe pre-eclampsia	6	37-40	6.0-14.5	11.62	3.33	192-227	238.3	29.20	1.90	>0.05 not significant
Eclampsia	4	37-40	3.0-9.0	5.8	2.78	182-288	237.2	48.45	1.23	>0.05 not significant
Postdate	10	41-42	9.5-24.4	15.8	5.80	184-234	203.1	14.49	2.81	<0.05 significant
Anaemia	20	37-40	8.6-20.75	12.61	3.38	188-242	208.25	19.72	2.07	<0.05 significant

Urinary oestriol was significantly low in cases of high-risk pregnancy, whereas serum copper was within the normal range in cases of I. U. G. R., toxæmia of pregnancy. Serum copper was however, found to be significantly low in cases of anaemia and postdate pregnancy.

similar to mean value obtained in normal pregnancy. Thus while urinary oestriol assays are helpful in arriving at a diagnosis which may be difficult on clinical grounds alone, the estimation of serum copper is of no value in the diagnosis of intrauterine growth retardation.

Mean serum copper in cases of mild pre-eclampsia was 222.9 ± 15.03 microgram/dl which was similar to that obtained in normal pregnancy ($p > 0.05$), whereas urinary oestriol excretion was 17.50 ± 5.02 mgm/24 hours, statistically significantly lower than the value obtained in normal pregnancy ($p < 0.05$). Moreover, in cases of mild pre-eclampsia urinary oestriol was remarkably low in those who delivered babies showing evidence of birth asphyxia and growth retardation, mean value being 11.16 ± 5.57 mgm/24 hours and 12.5 ± 4.41 mgm/24 hours respectively. But serum copper level did not show significant change ($p > 0.05$), mean value being 233.6 ± 6.66 microgram/dl and 226 ± 4.32 microgram/dl respectively. Thus measurement of oestriol output in 24 hours urine was found to be superior to serum copper estimation for assessment of placental

function. On comparing the value obtained in normal pregnancy serum copper level in cases of severe pre-eclampsia (238.3 ± 29.20 microgram/dl) and of eclampsia (237.2 ± 48.75 microgram/dl) were found to show insignificant change from the values obtained in normal pregnancy ($p > 0.05$). Urinary oestriol output on the other hand was found to be remarkably low in these cases and to correlate with severity of toxæmia, serum copper was within the normal limit in those cases of severe pre-eclampsia and of eclampsia who had intrauterine foetal death. Urinary oestriol however, was below 7 mgm/24 hours in these cases indicating thereby foetal jeopardy from before hand.

In cases of postdate pregnancy both mean urinary oestriol level (15.8 ± 5.8 mgm/24 hours) and mean serum copper level (203.1 ± 14.49 microgram/dl) were low as compared to those of normal pregnancy. But urinary oestriol was found to be a sensitive index of placental insufficiency as it showed significantly low value in those cases who delivered asphyxiated babies, whereas serum copper failed to reflect the intrauterine foetal jeopardy (Table III).

TABLE III

Comparison of Urinary Oestriol and Serum Copper Level Between Patients Who Delivered Asphyxiated Babies and Those Who Gave Birth to Healthy Babies in Postdate Pregnancies

Apgar score	No. of cases	Urinary oestriol in mgm/24 hours			Serum copper in microgram/dl		
		Range	Mean	S.D.	Range	Mean	S.D.
1-6	3	9.5-11.5	10.26	1.08	184-208	196.6	12.05
7-10	7	11.5-22.4	18.17	5.30	184-232	205.8	15.39
	't' value	2.29			0.32		
	'p' value	<0.05			>0.05		
	Remarks:	Significant			Not significant		

Urinary oestriol was significantly low in those patients who delivered asphyxiated babies as compared to those who delivered non-asphyxiated babies ('p' being <0.05). Serum copper was however, similar in both the groups ('p' >0.05).

TABLE IV
Urinary Oestriol and Serum Copper Level in Relation to Birth Weights in Pregnancy With Anaemia at Term

Birth weight in grams	No. of cases	Urinary oestriol in mgm/24 hours			Serum copper in microgram/dl		
		Range	Mean	S.D.	Range	Mean	S.D.
1600-2000 (Group I)	8	8.6-13.2	10.17	1.49	164-224	201.62	20.26
2100-2500 (Group II)	10	9.5-18.4	13.69	2.91	183-234	208.9	17.82
2600-3000 (Group III)	2	13.25 to 20.75	17.0	5.30	222-242	231.5	14.85
't' value	Between group I and II		2.93		0.76		
	Between group I and III		2.83		1.74		
'p' value	Between group I and II		<0.05		>0.05		
	Between group I and III		<0.05		>0.05		
Remarks:			Significant		Not significant		

Urinary oestriol was significantly low in "Low birth weight" babies, whereas serum copper showed no significant change ('p' >0.05).

In pregnancy complicated by anaemia urinary oestriol and serum copper levels were found to be low, the mean being 12.61 ± 3.38 mgm/24 hours and 208 ± 19.72 microgram/dl respectively. As shown in Table IV urinary oestriol was significantly low in "Low birth weight" babies 2000 grams or less, whereas no such correlation could be observed between serum copper level and birth weight of babies in anaemic mothers at term. In the light of above findings the broad conclusion which emerges from the present study is that urinary oestriol is a sensitive index of foeto-placental unit and its estimation is superior to serum copper estimation in the assessment of placental function.

Summary

Estimation of 24 hours' urinary oestriol and serum, copper was done in 80 cases of high-risk pregnancy and 20 cases of normal pregnancy. In the cases selected for study, duration of gestation varied

from 37 to 40 weeks except in cases of postdate pregnancies in which duration of gestation varied from 42 to 43 weeks.

In the light of present findings it can be reasonably concluded that urinary oestriol is a sensitive index of foeto-placental unit and its estimation is superior to serum copper estimation in the assessment of placental function.

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