

DIAGNOSTIC EVALUATION OF PREGNANCY URINARY OESTRIOL FOR FOETO-PLACENTAL FUNCTION

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Abstract

During pregnancy, the excretion of oestrogen increases enormously in comparison with the non-pregnant state but the striking feature of this increase is the great preponderance of oestriol as compared with oestrone and oestradiol. It is the foetus which plays a specific and essential role in the synthesis of oestriol and for this reason assay of the level of oestriol in maternal urine can provide information about the intrauterine conditions of the foetus. Serial urinary oestriol assays are carried out in 49 normal pregnant subjects and 5 subjects of obstetric complications. The oestriol values during normal pregnancy, $7.42 \pm 5.13\text{mg}/24$ hours at 1st trimester, $24.23 \pm 4.56\text{mg}/24$ hours at 2nd trimester and $33.00 \pm 9.87\text{mg}/24$ hours at 3rd trimester of gestation, have been calculated. The large deviations from these values showed some sort of disorders in the form of abortions, stillbirths, toxaeemias and ante-

partum haemorrhage (JPMA 29:209, 1979)

Introduction

The relatively large amounts of oestrogen excreted in the maternal urine during pregnancy, are derived almost entirely from the placenta. The placenta synthesizes these oestrogen from precursors which are produced largely in other sites, notably the foetus. Oestriol is quantitatively the most important urinary oestrogen and the measurement of this steroid provides useful information concerning the state of the foetoplacental unit. Greene et al. (1965) and Mcnaughton (1967) described some of the characteristic features of the state of foeto-placental units. A steady rise in oestriol value during gestation shows normal growth of the foetus while low oestriol values may provide information about stillbirths, perinatal death, mild antepartum haemorrhage and other obstetric complications.

Material and Methods

The 24 hours urine samples were collected on two to three consecutive days of each gestational week from 49 normal pregnant subjects and 5 abnormal subjects admitted for either routine check up and antenatal care or delivery at Sobhraj Maternity Home, Karachi. The urine samples were preserved in litre bottles containing 0.5ml formaldehyde and they were analysed within 3 to 4 hours. Serial determinations for oestriol values were made in order to minimise the day to day wide fluctuations in the content of oestriol.

Ten ml aliquot of heparinised 24 hour pregnancy urine is diluted to one litre with distilled water and then boiled. Fifteen ml of concentrated hydrochloric acid was added and the bulk solution was boiled again for one hour. The hydrolysate was cooled and transferred to a separating funnel and extracted with 30ml petroleum ether three times. The extract was washed with 20ml carbonate buffer and the aqueous phase was discarded. 5ml 2N sodium hydroxide was added, shaken and 20ml of 8% sodium bicarbonate was then added. The ether layer was collected, evaporated and the residue obtained was dissolved in 3ml of absolute alcohol. 50mg of hydroquinone was added to one ml of ethanolic solution. Standard oestriol in ethanol and blank (without hydroquinone) were also prepared. The ethanolic solvents were evaporated at 60°C , 2.6ml of Kober reagent was added

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during boiling and diluted with 0.7ml water. After development of colour both tests and standard solutions were read on Karl Zeiss spectrophotometer at 545nm for oestriol values against a reagent blank. Oestriol in pregnancy urine was then read over the calibration curve. The method of Hobkirk and Metcalfe-Gibson (1963) was adopted for this investigation.

Results

The primary oestriol excretion during normal pregnancy in a group of subjects of 20 to 40 years of age showed little rise till 1st trimester of gestation. A sharp rise in the amount of oestriol excretion from 7.42mg/24 hours is noticed onset 1st trimester i.e. 14.79mg/24 hours at 16th week, after the last menstruation period, during gestation. A pronouncing continuous rise in the amount of oestriol reached to 28th week of gestation and a maximum value of 33.60mg/24 hours was estimated at 36th week and later it was followed by a normal delivery of the baby. The mean oestriol values in normal pregnancy urine and standard deviation values have been tabulated (Table-I, Fig. 1).

The oestriol values in subjects who suffered from different obstetric complications have been summarised in Table-II.

Table-II: Oestriol Values in Subjects Suffering from Different Obstetric Complications

<i>Obstetric complications</i>	<i>Urinary Oestriol (mg/24 hour)</i>
Intrauterine foetal death	5 (at 27 weeks, Experimental) less than 5 (at 35 weeks, Miyakawa et al., 1976) " " 4 (at 35 weeks, Miyakawa et al., 1976)
Anencephalic pregnancy	9 (at 23 weeks, Experimental) 9.5 (at 31 weeks, Experimental) 10.0 (at 34, 35 weeks, Experimental) less than normal values (Miyakawa et al., 1976)
Toxaemia of pregnancy	greater than 49.9 and at term 129.8 (Miyakawa et al., 1976)
Twin pregnancy	less than normal values (Miyakawa et al., 1976)
Pregnancy complicated by hyperthyroidism	less than 8.0 (at term, Klopper, 1969)
Delivery of the baby is recommended	less than 16.0 (at term, Miyakawa et al., 1976)
suspicion of foetal and placental hypofunction	
<u>During Menstruation</u>	
Before ovulation	6 to 10Ug/24 hours (Ramos et al., 1968)
After ovulation	22 to 27Ug/24 hours

The mean urinary oestriol values in two of the subjects determined in this investigation showed 5mg/24 hours at 27 weeks of pregnancy while 6mg/24 hours at 32 and 36

Table-I: Urinary Oestriol Content During Normal Pregnancy

<i>No. of subjects</i>	<i>Gestational weeks</i>	<i>Oestriol values (mg/24 hour) Mean*</i>	<i>S.D.</i>
5	4	7.43	2.34
4	8	7.47	3.00
6	12	7.42	5.13
5	16	14.79	4.21
4	20	21.80	4.19
6	24	24.23	4.56
4	28	32.00	8.70
4	32	32.18	9.80
6	36	33.60	9.87

*Mean value of 2 to 3 determinations in 4 to 6 subjects, 19 to 35 years of age.

S.D. = Standard deviation of the mean oestriol values amongst subjects belonging to each gestational group.

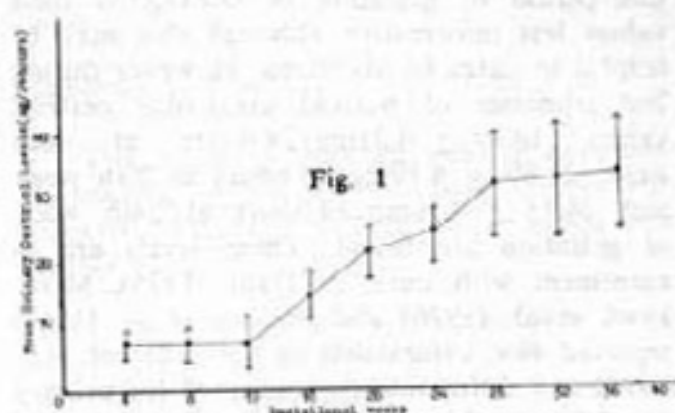


Fig. 1: Mean Urinary Oestriol Levels during normal pregnancy

weeks of pregnancy. Besides other endocrine factors very low oestriol excretion caused foetal death. In three of the toxæmic subjects the mean oestriol excretion assessed lie

in the range of 9 to 10mg per 24 hours during 23 to 35 weeks of gestation and thus provide information of foetal risks in jeopardy. Other cases of abnormality like encephalic pregnancy, pregnancy complicated by hyperthyroidism and twin pregnancy have been studied by other workers and their values are mentioned in Table-II. The mean normal non-pregnancy urinary oestriol values in women for comparison purposes were also studied (Table-II).

Discussion

During first trimester of normal gestation the oestriol values determined, lie in the range of 7.42 ± 5.13 mg/24 hours. Other investigators either did not report the values during this period of gestation or considered their values less informative although this may be helpful in cases of abortions. However during 2nd trimester of normal pregnancy oestriol values 14.79 ± 4.21 mg/24 hours at 16th week, 21.80 ± 4.19 mg/24 hours at 20th week and 24.23 ± 4.56 mg/24 hours at 24th week of gestation are found. These levels are in agreement with those of Dada (1975), Miyakawa et al. (1976) and Mcload et al. (1967) reported low values due to the different procedures of estimation they adopted for urinary oestriol excretion. Moreover the techniques of Miyakawa (1976) and Mcload (1967) are less sensitive for estimation of early pregnancy urinary oestriol values. At the 3rd trimester the values of oestriol lie in the range 32 ± 8.7 at 28th week, 32.18 ± 9.8 at 32nd week and 33.6 ± 4.87 mg/24 hours at 36th week of pregnancy. These values of normal pregnancy urinary oestriol are in agreement with Dada (1975), Miller and Weller (1971), Oakley et al. (1967) and Miyakawa et al. (1976). While Klopfer (1968, 1969) and Mcload et al. (1967) reported a little lower values of oestriol.

The oestriol values in abnormal pregnancy are considered as indication of disordered foetal and/or placental functions, since both the foetus and placenta are involved in oestriol production. Coyle et al. (1962) have reported foetal malfunctions during abnormal pregnancy and are caused by low oestriol excretions, genetic enzyme deficiency of placental sulphatase, cortisone therapy, foetal anencephaly, anaemia, hypertension, preeclampsia, renal diseases, diabetes and toxemia, the obstetric abnormality during pregnancy which leads to threatened abortions, mild antepartum haemorrhage, intrauterine perinatal death may atleast be detected by a fall in oestriol excretion. A rising level

of oestriol in the maternal urine is an indication of improvement in functions of foetal growth during pregnancy. It could be concluded that the declining level of oestriol excretion or values persistently below normal for the gestational age beyond 28th week, may indicate the need for immediate delivery of the baby. Furthermore, persistent toxemia during pregnancy causes low excretion of oestriol which is itself an indication to terminate pregnancy.

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