URINARY PREGNANEDIOL LEVELS IN INDIAN PREGNANT WOMEN*

by

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The exact significance of pregnanediol excreted in the urine during pregnancy is not yet well understood. Available reports (Sheerman, 1959; Klopper and Billewicz, 1963), suggest that large amounts of pregnanediol are excreted in the urine during pregnancy and they constitute about 15% of the progesterone elaborated by the placenta. The amount of pregnanediol in the urine does not, however, appear to be either related to progesterone levels in blood (Greig *et al.*, 1962), or to the birth weights of infants (Klopper *et al.*, loc. cit.) This has been explained as being due to the fact that pregnanediol is not an exclusive metabolite of progesterone.

Urinary excretion of oestrogens has been considered as reflecting placental function. Earlier reports from these laboratories (Iyengar, 1968) had shown that urinary oestrogen levels in undernourished pregnant Indian women were low and that there was a high degree of correlation between the birth weights of infants on the one hand and amounts of oestrogens in the urine on the other. Progesterone is the precursor of most of the steroids including oestrogens secreted during pregnancy. An investigation was, therefore, undertaken to study the excretion pattern of urinary pregnanediol, a major metabolite of progesterone, in undernourished pregnant women. This was done in an attempt to define the extent to which the placenta contributed to the lowered steroid synthesis in undernourished pregnant subjects. Since it is known that the levels of steroid hormones in urine show a steep rise after 28 weeks of pregnancy, the determination of pregnanediol levels was done on samples of urine obtained after 28 weeks of gestation.

Material and Methods

Twenty-four hour and single morning samples of urine were collected without any preservative from 42 pregnant subjects belonging to the low income group between 28 and 40 weeks.

A single morning urine sample was collected from 94 other pregnant women, who were between 28 and 40 weeks of gestation. These women attended the antenatal clinic of the Niloufer Hospital, Hyderabad, and belonged to the low income groups with an average monthly income of Rs. 100 or less. The habitual diets of these women provided around 40 gms. of proteins from vegetable sources and 1600 to 1800 calories daily. The urine samples were stored at 4°C

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Received for publication on 24-6-1969.

till analysed, which was done usually within 7 days of collection. Similar collections of urine samples were made from 67 pregnant women belonging to the upper income group who attended an army hospital near Hyderabad. These women were wives of army officers with an average monthly income of over Rs. 1,000. The diets of these women provided around 100 gms. of proteins and 2500 calories daily.

Pregnanediol in urine was determined by the modified method of Bang (1964), using thin-layer chromatography. After separating the pregnanediol, the colour was developed with sulphuric acid and read at 430 $m\mu$ in a Beckman D.U. Spectrophotometer. Creatinine was determined by the method of Folin (1914), and the values for pregnanediol expressed as mg/gm. creatinine.

Results

A high degree of correlation was seen between the values for pregnanediol obtained on single morning urine samples and the 24 hours urine samples. ($P < 0.001$, $\alpha = 0.9520$) Fig. 1).

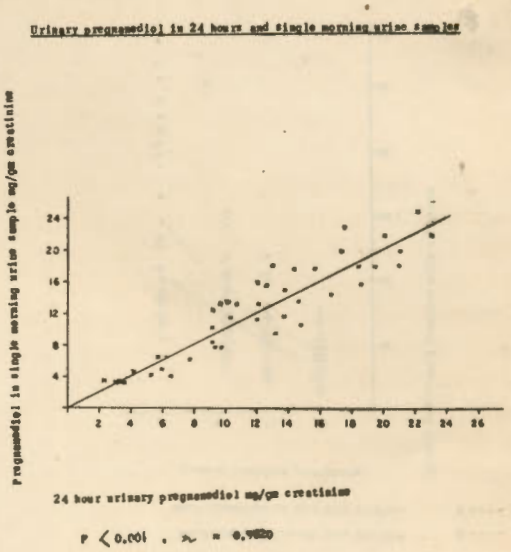

Fig. 1

The levels of urinary pregnanediol between 28 and 40 weeks of gestation (Table 1 and Fig. 2) showed an increase with increasing gestational period, the peak value being at 40 weeks. There was, however, a wide scatter of values at each gestational period.

TABLE I

Urinary pregnanediol levels in Indian pregnant women

Income group	Weeks of gestation			
	28	32	36	40
Low	7.2 ± 0.63 (19)	10.3 ± 0.9 (23)	14.8 ± 1.07 (35)	21.4 ± 2.32 (17)
High	8.8 ± 1.06 (13)	13.7 ± 1.80 (13)	18.4 ± 1.64* (18)	30.2 ± 3.25* (23)

Values are means ± S.E.
No. of subjects given in parenthesis.
* $P < 0.05$.

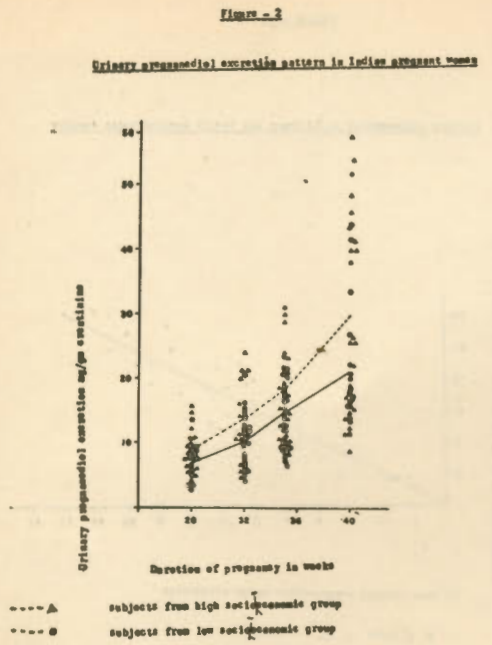

Fig. 2

The levels of pregnanediol in women belonging to the higher income group were higher than those in women of the low income group, though the difference was statistically significant at 36 and 40 weeks ($P < 0.05$).

No correlation was seen between the birth weights of infants and pregnanediol levels in urine at term.

Discussion

Determination of levels of oestrogen and pregnanediol in urine has been widely used for following the course of pregnancy. Level of pregnanediol in urine is considered to be an index of progestational activity of placenta, since its precursor progesterone is synthesized *de novo* in large quantities in the placenta (Ryan *et al*, 1966). However, varying results were obtained by Macnaughton (1966) in conditions of habitual abortions and placental insufficiency, when he tried to assess placental function using urinary pregnanediol level as the parameter. Therefore, the use of this hormone alone in prognosticating the course of pregnancy in abnormal conditions has been questioned.

The high degree of correlation observed between the excretion in single morning sample and 24 hour excretion of pregnanediol is of clinical significance, since it obviates the necessity to obtain 24 hour urine samples and the assays can be done in a routine antenatal clinic on single morning urine samples.

The results obtained here have shown that as in the case of oestrogens, the amount of pregnanediol in urine is lower in undernourished women. This seems to indicate a low progesterone production by the placenta in undernourished states. Greig *et al* (1962) have found that the correlation between blood progesterone and urinary estriol is closer than that between blood progesterone and pregnanediol, indicating thereby the metabolic inter-relationship between progesterone and oestrogens.

The synthesis and metabolism of oestrogens during pregnancy depends on an intact feto-placental unit, since the foetus supplies the precursors for the placenta to synthesize oestrogens. For the synthesis of progesterone and its conversion to pregnanediol, the foetus plays a very minor role, as is shown by the fact that in cases of anencephaly, pregnanediol excretion is normal even though oestrogen excretion is very low. Earlier, it was suggested that low oestrogen excretion in undernourished pregnant

women could be explained on the basis of either a diminished supply of precursor by the foetus to the placenta or an inefficient conversion of the precursor to oestrogens by the placenta in conditions of malnutrition (Iyengar, 1967). The observation that as in the case of oestrogen, the amount of pregnanediol in urine is also low in undernourished pregnant women indicates that it is the placental function that may be defective in such women.

Though the levels of urinary pregnanediol are significantly higher in the well-to-do women as compared to the undernourished subjects, they appear to be considerably lower than the levels reported for pregnant women in the West by Sheerman (1959) and Klopper *et al* (1963). This is surprising in view of our earlier observation that the urinary estrogen levels in wellnourished Indian women are similar to values reported for Western women. The reasons for this observation need elucidation.

Summary

(1) Pregnanediol levels in the urines of pregnant subjects were determined by using thin layer chromatography.

(2) A close correlation was observed in the levels of pregnanediol in single random morning urine samples and twenty-four hour urine samples.

(3) The levels of pregnanediol in urine were significantly lower in undernourished pregnant women at term, as compared to levels in well nourished pregnant women, suggesting sub-optimal placental function.

Acknowledgment

The author is grateful to Dr. S. G. Srikantia, Deputy Director, and Dr. C. Gopalan, Director, for their interest and guidance in this study. She acknowledges gratefully the help of the medical staff of Air Force Hospital, Trimulghery, Secunderabad, in this study. She extends her appreciation to Mr. Syed Mohammed for the technical assistance.

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