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A Longitudinal Study of Thyroid Function in Saudi Pregnant Women

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ABSTRACT. A prospective longitudinal study of thyroid function was undertaken in 23 pregnant women. There was significant increase in serum free thyroxine and a decrease in thyrotropin in early pregnancy relative to the levels in non-pregnant controls. Free thyroxine significantly correlated with human chorionic gonadotrophin in early pregnancy. The level of decreased and that of thyrotropin increased significantly towards the end of pregnancy. On follow-up of pregnant women, thyroid function returned to normal 6 weeks post-partum. These data indicate that the thyroid gland is physiologically activated in early pregnancy, possibly by human chorionic gonadotrophin.

Keywords: Thyroid Function, Pregnancy, Saudi, Thyrotropin, Human Chorionic Gonadotrophin.

Introduction

Increased concentration of thyroxine (T4) and triiodothyronine (T3) due to increased thyroxine-binding globulin (TBG) have been widely described in pregnancy[1]. Free T4 (FT4) concentration reflects thyroid functional status more accurately[2]. Maternal FT4 concentration has been variously reported by several studies to be unchanged, decreased or increased[3]. These discrepant results may have been partly due to the use of different assay methods[4,5]. Several lines of evidence have suggested that the thyroid gland activated in early pregnancy. At this time, the level of serum FT4 increases and serum thyrotropin (TSH) decreases[6,7] and in the thyroid gland, follicles enlarge and the cells show hypertrophy[8].

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In normal pregnancy three kinds of thyroid stimulators have been reported namely: pituitary TSH, chorionic TSH, and hCG[4]. hCG, which increases to a maximum level in pregnancy, seems most likely to stimulate the thyroid gland in early pregnancy, but discrepant results have been obtained regarding its thyrotropic gland activity[8]. The present work describes a prospective longitudinal study of thyroid function during each trimester of pregnancy and six weeks postpartum. The pattern of changes in hCG were compared with that of thyroid function tests during the three trimesters and the post-partum period.

Material and Methods

Thirty five pregnant women in good health (age range 19-36 yrs) were randomly selected and were attending the antenatal clinic in King Abdulaziz University Hospital, Jeddah. The selected group had no history or symptoms of thyroid dysfunction and taking medication only for minor complaints unconnected with thyroid disease. The only medication given during pregnancy was anti-anemia therapy. Pregnancy was uncomplicated with normal outcomes and recovery. Out of 35 only 23 women could be followed-up starting from the first trimester till the end of the study. The sampling times for each trimester were: first trimester (6-13 weeks) (gp 1), second trimester (14-26 weeks) (gp2), and third trimester (27-40 weeks) (gp3). The pregnant women were followed-up and a sample was taken at 6 weeks postpartum (gp4).

For every pregnant woman in each trimester 10ml of blood samples were taken with no additives. Serum was separated within two hours, frozen immediately and stored at -20° C until analyzed.

The study also involved 17 non-pregnant women (age range 22-23 yrs) who were selected as controls (gp0). They were healthy or affected with non-thyroid illnesses of no severity and not being known to be taking any medications which might affect the measurements. Blood samples were collected and treated in the same way as described above.

FT4, and hCG were measured by time- resolved flourimmunoassay method using a commercial kit available from Pharmacia Co. (Copenhagen, Sweden).

FT3 and TBG was measured using radioimmunoassay. The kits were supplied by Ammersham International PLC (Ammersham,UK). Albumin was measured by Hitachi auto-analyzer. The sensitivity and intra-,and inter-assay variations of this FT4 assay were 0.25 pmol/l and 4.6-8.6 and 6.1-11.5%, respectively. The sensitivity and intra- and inter-assay variations of TSH assay were 0.13mol/l and 0.8-4.2 and 1.7-13.0%, respectively. The sensitivity and intra- and inter-assay variations of hCG assay were 0.3 mol/l and 2.5-4.6 and 0.5-6.1%, respectively. The sensitivity and intra-,and inter-assay variations of FT3 assay were 0.3 pmol/l and 3.5-7.8 and 5.8-9.5%, respectively. The sensitivity and intra-and inter-assay variations of this TBG were 0.15 mg/l and 3.2-5.4 and 2.1-8.0%, respectively. Data were analyzed using students *t*-test to compare all the results for control values. The correlation between two variable was studied by linear regression analysis.

Results

Serum levels (Mean±SE) of FT4, TSH, FT3, hCG, TBG and albumin of 23 pregnant women, together with their respective levels of age-matched non-pregnant women are presented in Table 1.

TABLE 1. The levels of serum thyroid hormones, thyroid stimulating hormone, human chorionic gonadotrophin, thyroxin - binding globulin and albumin of pregnant women during and after pregnancy and non- pregnant control.

Group	FT4 (pmol/1)	TSh (MU/1)	FT3 (pmol/1)	hCG (IU/1)	TBG (mg/1)	Albumin (g/l)
Control	13.7 ± 0.3	1.3 ± 0.1	4.9 ± 0.5	2.0 ± 0.4	21.5 ± 0.8	42.0 ±1.2
1st trimester	15.6 ± 0.5*	1.4 ± 0.2	6.0 ± 0.2	16239 ± 417*	34.1 ± 3.3*	41.6 ± 1.3
2nd trimester	13.7 ± 0.5	1.8 ± 0.3	5.1 ± 0.2	13047 ± 841*	50.5 ± 2.3*	40.2 ± 0.9
3rd trimester	11.2 ± 0.3*	2.3 ± 0.2*	4.6 ± 0.1	10314 ± 1007*	58.4 ± 4.1*	36.2 ± 0.9*
Postpartum	13.3 ± 0.4	1.7 ± 0.2	5.9 ± 0.1	5.2 ± 7.8	20.4 ± 0.7	47.2 ± 0.7

Data are presented as Mean ± SE
*P < 0.005 significant as compared to control.

Changes during pregnancy: The FT4 levels in early pregnancy were significantly higher than the FT4 levels of non-pregnant women; being 15.6 ± 0.5 pmol/l (6-13 weeks); 13.7 ± 0.3 pmol/l (non-pregnant, P < 0.005), respectively. Although FT3 levels in early pregnancy remained in the upper limits, did not exceed significantly those of non-pregnant women values. TSH levels did not show a significant change in early pregnancy. The level of FT4 in late pregnancy (27-40 weeks) were significantly lower than that of the FT4 levels of non-pregnant women; 11.2 ± 0.3 pmol/l, 12.7 ± 0.3 pmol/l (non-pregnant) (P < 0.005), respectively.

The levels of hCG were highest in the early period of pregnancy (6-13 weeks). This was followed by a gradual decline in the middle and late period of pregnancy. The pattern of change of hCG was significantly different (P <0 .005). The levels of TBG progressively increased during pregnancy and maintained a plateau in the subsequent periods. The pattern of change was significant when compared with non-pregnant controls. The levels of albumin were not significantly different except in late period where values decreased significantly when compared to non-pregnant levels; 36.2 ± 0.9g/l, 42 ± 2g/l (non-pregnant) (P < 0.005), respectively.

Changes after pregnancy: The levels of T4, T3, TSH, hCG and albumin were tested in post-partum period (6 weeks). The levels of almost all analyses measured returned to non-pregnant values.

Correlations between changes of two variables: For the first trimester T4 levels correlated positively with hCG levels (r = 0.35, P<0.05) (see Fig.1). For all sera T4 and albumin estimates were strongly correlated (r = 0.46, P < 0.001) (Fig. 2). For all sera FT4 and TSH levels were negatively correlated (r = 0.44, P < 0.005) (Fig. 3).

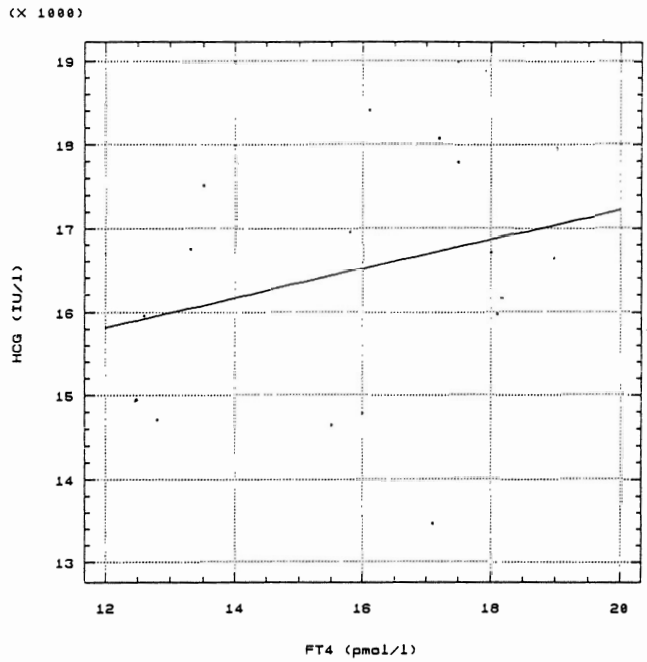

FIG. 1. Correlation of FT4 and hCG during 1st trimester (r = 0.35; P < 0.05)

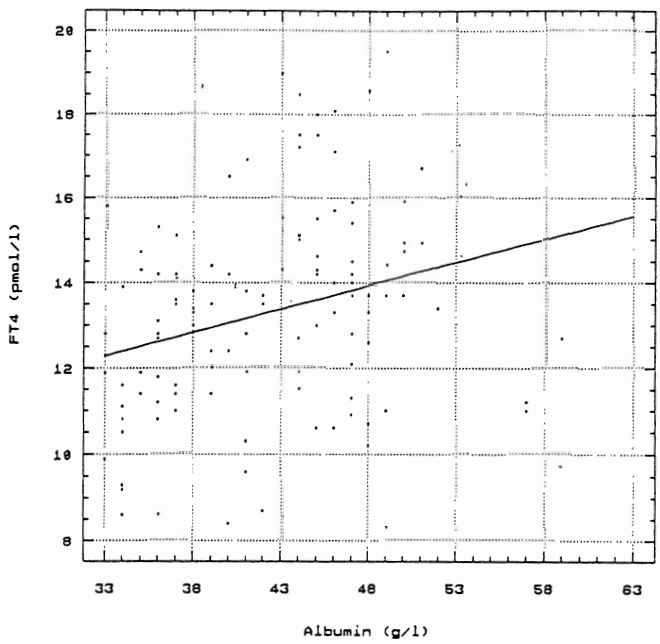

FIG. 2. Correlation of FT4 and albumin for all sera (r = 0.4; P < 0.001).

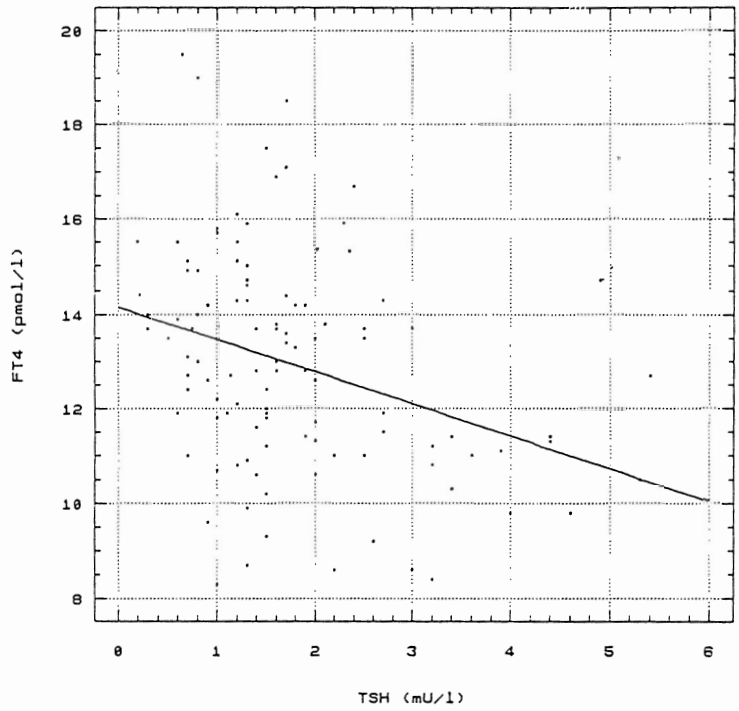

FIG. 3. Correlation of FT4 and TSH for all sera (r = 0.44; P < 0.005)

Discussion

In the present study, the levels of FT4 were significantly increased above the corresponding values of non-pregnant women in the early period and less so in the later period of pregnancy. FT3 levels were elevated only in the early weeks of pregnancy. These changes are consistent with other reports[4,9-11]. The elevated levels of T4 and FT3 have to be maintained either by hypersecretion of thyroid hormones or, in the case of FT3 by augmented conversion of FT4. TSH changed reciprocally with FT4. Its concentration in early pregnancy was usually low. The elevated levels of FT4, FT3 in conjunction with increased levels of hCG which were significantly correlated with FT4 and slightly decreased levels of TSH in the early period of pregnancy led to speculation that the thyroid gland might be stimulated during this period, at least in part by hCG[12]. Kimura *et al.* [4], demonstrated *in vitro* a close relationship between thyroid stimulating activity and serum hCG levels. The thyroid-stimulating activity was abolished by immune absorption of hCG antibody; the latter clearly indicating that hCG itself has intrinsic stimulatory activity. Though high hCG levels in early pregnancy could augment TSH activity *in vivo*[13]. Hence, to maintain normal FT4, hypothalamus-pituitary-thyroid feedback control may require less TSH. In late pregnancy, hCG levels decline, allowing TSH to resume its usual regulatory potency[14]. Serum FT4 in late pregnancy thus seems to mimic mild compensated hypothyroidism[15]. It is possible therefore that physiologic thyroid stimulation by circulating hCG in early pregnancy may be an important

adaptive changes to maintain progress of conception. A slight increase in FT4 might activate many cells in different organs appropriately to maintain pregnancy[16].

Thyroid hormones are carried in the blood bound to proteins (TBG, albumin, thyroxine-binding prealbumin). The natural decrease in the albumin concentration in serum during pregnancy and the changes in serum FT4 were physiological and were not explained by technical artifact[1]. FT4 measurements appeared not to be affected by changes in TBG concentrations, because there were no significant correlations between FT4 and TBG.

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دراسة وظيفة الغدة الدرقية خلال الحمل لنساء سعوديات

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المستخلص . عملت دراسة لوظائف الغدة الدرقية أثناء الحمل وبعد الولادة لثلاثة وعشرون سيدة حامل . وظهر أن هناك ارتفاع واضح في مستوى FT4 وانخفاض مستوى هرمون TSH وذلك خلال الفترة الأولى من الحمل والمقارنة تمت على مستوى هرمونات الغدة الدرقية لسيدات غير حوامل . كما ظهر أن هناك علاقة واضحة بين مستوى هرمون FT4 وهرمون hCG أثناء الفترة الأولى من الحمل . ولقد وجد أن مستوى FT4 قد انخفض وازداد مستوى TSH بشكل بيِّن في الفترة الأخيرة من الحمل . وبمتابعة الحوامل بعد الولادة بستة أسابيع وجد أن مستوى هرمونات الغدة عاد إلى مستواه الطبيعي . تؤكد النتائج السابقة أن الغدة الدرقية تنشط أثناء الفترة الأولى للحمل وقد يكون أحد العوامل المنشطة هو هرمون hCG .