Original Article

Thyroid Stimulating Hormones (TSH & hCG) and thyroid functions in normal pregnancy

Rahman MH[1], Chowdhury MA[2]

Abstract

Hormonal changes and maternal demands during pregnancy result in marked changes in maternal thyroid activity. It has been suggested that the thyrotropic effect of hCG in pregnancy increases thyroid activity in addition of thyrotropic effect of TSH. To compare the serum levels of thyroid stimulators (hCG & TSH) and thyroid hormones (T3 & T4)) in normal pregnant women and thus to clarify the role of hCG & TSH on thyroid function in pregnancy, we measured serum hCG, TSH, total T3 & T4 and free T3 & T4 concentrations in the serum samples of 32 pregnant women in their different trimesters and in the serum samples of 22 non-pregnant normal female control. Serum total T3 & T4 were significantly elevated throughout pregnancy in comparison with controls. Free T4 level was elevated at 1st trimester but reduced in 2nd and 3rd trimesters. The free T3 levels were remained unchanged throughout pregnancy and no significant change in pregnancy than non pregnant control. Serum TSH levels were significantly lower at 1st trimester compared to 2nd and 3rd trimester of the pregnancy. Serum hCG levels were highest in 1st trimester. We conclude that hCG, as a weak thyroid stimulator, causes moderate increase in free thyroid hormone levels in 1st trimester which in turn causes a moderate reduction in TSH levels in early pregnancy.

Key Words: *Pregnant, hCG, TSH.*

Introduction

Pregnancy is a physiological process where maternal physiological adjustment of different organ system occurs including circulatory, metabolic and hormonal adjustments to supply adequate nutrition to the growing fetus[1]. The thyroid gland adjusts its activity to the increased demands of pregnancy by alterations in the biochemical parameters of thyroid function. It increases its secretion as well as size in pregnancy. In normal person these types of changes in thyroid gland may be suggestive of thyrotoxicosis, but in pregnancy, these findings are neither accompanied by sign-symptoms of thyrotoxicosis nor associated with metabolic demand especially in early pregnancy[2]. Thyroid secreation is controlled primarily by TSH which is secreted by anterior pituitary gland. During pregnancy, there is evidence for the presence of three thyroid stimulators, the pituitary thyroid stimulating hormone (TSH), the human chorionic gonadotropin (hCG) hormone, the chorionic TSH (hCT). However, data about serum levels of hCT is conflicting[3]. Some studies could not detect it, while others have reported significant level of circulating hCT in pregnancy[4,5]. During pregnancy thyroid gland increases its size and alters its functional parameters. On the other hand increased thyroid binding globulin (TBG) level in pregnancy results increased serum binding capacity and thus indirectly enhances thyroid secretion. Therefore maternal thyroid is regulated by different factors. Data indicate that hCT is not a significant thyroid stimulator[3]. The hCG of placental origin due to its structural and functional similarity with TSH exerts same thyrotropic effect on maternal thyroid gland as TSH. The high levels of circulating hCG observed in early pregnancy have been-

1. Dr. Md. Hafizur Rahman, Assistant Professor, Department of Physiology, Rajshahi Medical College.
2. Dr. Mahbub Ara Chowdhury, Junior Consultant (Gynae & Obst), OCC, Rajshahi Medical College Hospital.

Correspondence: Dr. Md. Hafizur Rahman, Assistant Professor, Department of Physiology, Rajshahi Medical College, Cell 01718824400

found to correlate negatively with TSH. This elevated hCG levels during the 1st trimester and the lower TSH level often observed early in pregnancy do raise the possibility of some degree of thyroid hyper function in early pregnancy. To evaluate the role of these thyroid stimulators in the control of thyroid function in normal pregnancy, the present study had the following objectives:1) measurement of serum levels of hCG & TSH in different trimesters; 2) measurement of serum total T3 & T4and free T3 & T4 levels; and 3) correlation of the circulating thyroid hormone levels with those of the thyroid stimulators. In the present study serum total T3 & T4 levels were significantly elevated throughout pregnancy in comparison with controls. Free T4 level was elevated at 1st trimester and free T3 did not show any significant change in pregnancy in compare to non pregnant control. Serum TSH levels were significantly lower at 1st trimester compared to 2nd and 3rd trimester of the pregnancy. Serum hCG levels were highest in 1st trimester and serum TSH levels were highest in 3rd trimester.

Materials And Methods

The study was conducted in the department of Physiology, Rajshahi Medical College with collaboration of the department of obstetrics and gynecology, Rajshahi Medical College Hospital. The total duration of this study was 12 months. Age ranged from 18 to 35 years and a total of 54 subjects were selected among which 32 normal women were studied during the course of pregnancy and 22 non pregnant female control; 10 ml of venous blood samples were taken from each of the 32 normal pregnant women in the 1st trimester (8-12 weeks of gestation), 2nd trimester (16-23 weeks), 3rd trimester (32-38 weeks) and from 22 non pregnant normal female control. All subjects were healthy with no family history of thyroid disease and were clinically and biochemically euthyroid. No evidence for iodine deficiency was apparent. Informed consent was obtained from all subjects. Total T3 (TT3), total T4 (TT4), free T3 (FT3), free T4 (FT4), TSH and hCG were measured. Serum T3 and T4 were measured by conventional RIA method. Serum TSH was measured by a sensitive RIA. Serum hCG was measured by RIA with an antibody directed against the-subunit. The reagent kits used were manufactured by Beijing Atomic High-tech. Co. Ltd. China.

Results

Serum TT3 and TT4 were expressed in nmol/L and serum FT3 and FT4 were expressed in pmol/L. Serum TSH was expressed in mU/L and serum hCG was expressed in IU/L. The results were presented as mean±SE (standard error of mean).

Table1: Biochemical parameters of thyroid function.

Parameters	Normal value/unit	1^{st}trimester mean ±SE	2^{nd}trimester mean±SE	3^{rd}trimester mean±SE	Non pregnant control mean±SE
hCG	(IU/L $\times 10^3$)	38.5 ± 1.5	16.4 ± 0.9	13.0 ± 1.5	undetectable
TSH	(0.2 -4.0 mU/L)	0.75 ± .04	1.05 ± .04	1.29 ± .04	1.22 ± .04
TT_4	(50 -150 nmol/L)	137.0 ± 3.0	148.0 ± 3.0	147.0 ± 3.0	78.0 ± 3.0
TT_3	(1.40-3.20 nmol/L)	3.15 ± .03	3.55 ± .05	3.58 ± .03	1.8 ± .03
FT_4	(10 -26 pmol/L)	17.9 ± 0.3	14.5 ± 0.1	13.4 ± 0.1	14.3 ± 0.1
FT_3	(3.0 –II.0pmol/L)	4.8 ± 0.1	4.2 ± 0.1	3.8 ± 0.1	3.1 ± 0.2

TSH & hCG

hCG levels peaked in the 1st trimester, 38.5 ± 1.5 (mean±SE) IU/L and then decreased, 16.4 ± 0.9 & 13.0 ± 1.5 IU/L in the 2nd and 3rd trimesters respectively. In non pregnant control, hCG levels were undetectable in all cases ($\leq$ 2 IU/L). A significant decreased in TSH was observed (0.75 ± .04 IU/L) in the 1st trimester of pregnancy in comparison to 2nd (1.05 ± .04 IU/L) and 3rd (1.29 ± .04 IU/L) trimesters and non pregnant control (1.22 ± .04). A significant negative correlation between TSH and hCG levels was observed in the 1st trimester. But not in the 2nd and 3rd trimester. TSH levels were lower in the 1st trimester than non pregnant control.

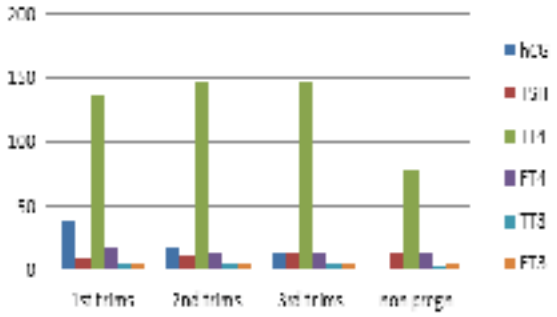

Fig 1. Bar diagram showing parameters of thyroid function.

TT3 & TT4

TT3 levels progressively increased throughout pregnancy and were significantly higher in all the three trimesters than non pregnant control (see Table 1). TT4 levels increased significantly in the 1st trimester of pregnancy and remained elevated in the rest of the pregnancy.(see Table 1). Basal TT3 and TT4 levels were in the normal range. No significant correlation was found between hCG and TT3 & TT4 levels throughout pregnancy.

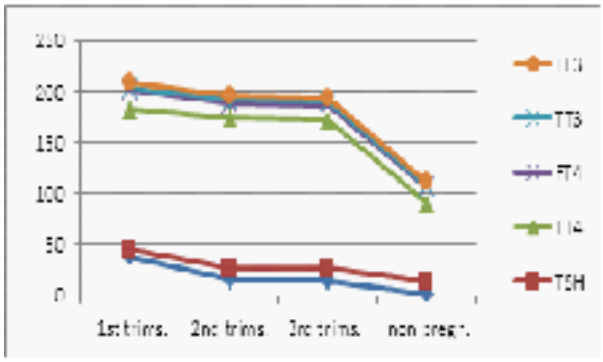

Fig 2. Line diagram showing relation between parameters of thyroid function

FT3 & FT4

There was no significant difference in mean serum FT3 levels between trimesters as well as between pregnant and non pregnant control. Although basal serum FT4 levels were within normal rage in most of the subject throughout pregnancy, in 2 subjects, 1st trimester FT4 levels were higher than normal range. Mean serum FT4 level was significantly decreased in 2nd and 3rd trimester in comparison to 1st trimester level. No significant correlation was found between hCG and FT4 levels throughout pregnancy.

Discussion

The present study represents an evaluation of thyroid hormone levels in different trimesters of gestation and the correlation between thyroid hormones and thyroid stimulating hormones throughout normal pregnancy. We have focused our attention on detecting the serum hCG and TSH levels in different stages of pregnancy and the changes in total and free thyroid hormone levels due to their thyrotropic effects on maternal thyroid gland. In some studies, the serum TSH levels have been showed higher or unmodified in early pregnancy[6]. In other studies, TSH levels were significantly decreased at a time when hCG levels were highest early in pregnancy[7]. There is controversy especially on free hormone levels in different studies. The choice of analytical sound method and reagents for measuring the hormones is critically important. Our results are consistent with many other reports. We found a decreased in TSH in 1st trimester of pregnancy and a return to normal in the 2nd and 3rd trimesters which is associated with rise of hCG in early pregnancy. It is suggestive that any control mechanisms governing the alteration in thyroid function other than pituitary TSH are in early pregnancy. The increased thyroid activity in early pregnancy did not appear to be due to TSH which is decreased in early pregnancy. The early enhanced thyroid activity does not sustained in rest of the period of gestation. The TT4 levels significantly increased in the 1st trimester, reaching a sustained level thereafter. We observed in this study a significant negative correlation between TSH and hCG levels in the 1st trimester. These findings are consistent with the well known TSH-like activity of hCG[8] and support the hypothesis that an alternative control system may operate maternal thyroid activity in early pregnancy when most important change in TT4 secretion occur.

FT4 levels do not differ from control values in the 1st trimester, but decreased in the 2nd and 3rd trimester. Some studies showed discrepancies with the present study where FT4 has been described as increased[3,9]. Such variation may be reflected as the inaccuracy of the different methods used for FT4 measurement. In our finding, the unchanged FT4 levels in the 1st trimester which is associated with decreased TSH, probably suggestive of adjunctive effect of hCG with TSH. In this study, serum TT3 levels were significantly higher in all three trimesters of pregnancy than that of non pregnant control whereas FT3 levels remained similar with the control group. The increased in serum binding forms of thyroid hormones may be due to the marked increase in circulating level of the major thyroid binding protein (TBG), which is induced by high estrogen level in pregnancy.

Conclusion

Study should the thyrotropic regulation of the maternal thyroid is complex and unclear resulting from effect of both hCG and TSH in pregnancy and changes in throid volume as well as elevated TBG. The present study is providing additional arguments as the hCG is a thyroid stimulator; in early pregnancy increased levels of hCG produces thyroid stimulating activity in addition of TSH effect results in moderate rise in free thyroid hormone levels. The increased level of hCG causes moderate reduction in pituitary TSH level. As pregnancy proceed, the secretion of hCG falls, there is a return of normal TSH and thyroid hormone secretion.

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