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Research Article

Thyroid Status in Non-Pregnant & Pregnant Women

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Abstract: Pregnancy is associated with significant, but reversible changes in thyroid function studies, which are among the most profound seen as a result of a normal physiologic state. Thyroid hormones have important role in embryogenesis and fetal development during pregnancy. Therefore, thyroid status is frequently assessed during pregnancy, both to evaluate suspected thyroid abnormalities, and to monitor the status of pre-existing thyroid disease. The aim and objective of the study was to compare thyroid function test in each trimester in normal pregnant women with non pregnant women. A case-control study containing two groups of women,75 normal pregnant women as cases selected from the first trimester (25 samples), the second trimester (25 samples), and the third (25 samples) trimester and 75 randomly selected non-pregnant healthy female controls. Thyroid function tests were carried out by measuring the serum levels of thyroid stimulating hormone (TSH), free and total thyroxin (FT4, T4), and free and total triiodothyronine (FT3, T3) by commercially available radio-immunoassay kit. The statistical significance was evaluated by Student's t-test. p value <0.05 was the level of statistically significance. In the third trimester, the mean TT4 increased significantly than the mean of non-pregnant women. The mean TT3 levels of pregnant women was increased in the second trimesters, and declined in the third trimester than the mean of non-pregnant women. In the third trimester, the mean FT4 significantly decreased than the mean for non-pregnant women. Mean FT3 values showed declining over the trimesters relative to the non-pregnant control group that were significant in second and third trimesters. In each trimester, the mean TSH levels of pregnant women were lower than the mean level of non-pregnant but were not statistically significant in second and third trimesters. The thyroid function tests in pregnancy should be interpreted against gestational age-related reference intervals in order to avoid mis-interpretation of thyroid function during pregnancy.
Keywords: Pregnancy, Thyroid stimulating hormone (TSH), Free thyroxine (FT4), Total thyroxin (T4), Free triiodothyronine (FT3), Total triiodothyronine (T3).

INTRODUCTION

Normal pregnancy results in a number of important physiological and hormonal changes altering thyroid function. In last twenty years, major expansion of our knowledge has taken place regarding the relationships between pregnancy and the thyroid hormones. The most important finding include maternal thyroid hormones play a vital role in early fetal brain formation, and their deficiency may impair future neuropsychological development of the fetus [1–3]. Pregnancy is associated with certain physiological changes and the maternal thyroid gland has to adapt accordingly [1, 4]. The first factor is the adjustment of bound to free ratio of T_4 and T_3 against the marked increase in the circulating levels of thyroxin binding globulin (TBG) levels due to enhanced estrogen production. The second factor is the direct stimulation of the thyroid gland by elevated concentration of human chorionic gonadotropin (hCG). These two factors occur in the first trimester of pregnancy [1]. The third factor is the increased enzymatic activity of type III monodeiodinase. It converts T_4 to reverse T_3 (rT_3) and thus increases the turnover rate of maternal T_4 at the placental level, operative in later stages of pregnancy [1, 4]. During pregnancy maternal iodine requirement increases which is further increased due to increased renal clearance of iodine. Moreover, a part of the available iodine from the maternal circulation is diverted to fetal thyroid gland which becomes progressively functional by the end of the first trimester [1, 4]. Thus, the regulation of maternal thyroid function is complex and varies with each stage of pregnancy [1]. Moreover, human chronic gonadotropin (hCG) can stimulate the thyroid gland during first trimester because of its structural similarity to thyrotrophin (TSH) [5]. Both normal pregnancy, and pregnancy

complicated by conditions like hyperemesis gravidarum (HG) that can be associated with thyroid function study changes, strongly suggestive of hyperthyroidism, in the absence of primary thyroid disease [6-8]. Thus, a local reference range for thyroid hormones in pregnant women is essential [9-14]. The availability of gestational age-dependent reference intervals for thyroid hormones for local population should help to avoid the under diagnosis of hyperthyroidism or the over diagnosis of hypothyroidism, with inadvertent use of thyroxine replacement in later pregnancy, also allowing an accurate interpretation of thyroid hormone results in complicated pregnancies, which may have abnormal thyroid function, such as pre-eclampsia and HG [9, 11, 14]. Therefore, we conducted a study to find out alterations in thyroid function tests in each trimester in normal pregnant women as compared to non-pregnant women.

MATERIALS AND METHODS

The present study was carried out at Hassan institute of Medical science, Hassan . 150 subjects (75 cases and 75 controls) were taken for the study Age range in both groups was 16-40 years A case-control study containing two groups of women,75 normal pregnant women as cases selected from the first trimester (25 samples), the second trimester (25 samples), and the third (25 samples) trimester and 75 non-pregnant healthy female at childbearing age are taken as controls. Pre-existing thyroid disease, hyperemesis gravidarum, trophoblastic disease, or preclampsia are excluded from the study. All subjects were consuming iodide salt. Therefore, no one of the subjects had iodide deficiency problem. After obtaining informed written consent from the study subjects and maintaining all aseptic precautions, 5 ml of blood were collected between 6 to 7 am from both cases and control group. Then, thyroid function tests carried out by measuring serum levels of thyroid stimulating hormone(TSH), free and total thyroxin (FT4, TT4), and free and total triiodothyronine (FT3, TT3) using commercially available radio immunoassay kits.

Statistical analysis

All data were expressed as mean ± SD of number of experiments. The statistical significance was evaluated by Student's t-test using SPSS version 10.0. p value <0.05 was the level of statistically significance.

RESULTS

Mean age was not significantly different between the groups (p=0.08). Pregnant women had a significantly increased body mass index compared to non-pregnant women (p<0.0001).

Table 1: Demographic characteristics

Parameters	Non-pregnant women	Pregnant women	p-value
Age (years)	23.5 ± 12.4	26.8 ± 10.2	p=0.08
BMI	25.6 ± 3.1	31.3 ± 5.8	p<0.0001

We found that in the first and second trimesters, the mean TT4 levels of pregnant women were increased but not statistically significant. However, in the third trimester, the mean TT4 increased significantly than the mean of non-pregnant women. The mean TT3 levels of pregnant women were increased in first trimester but not statistically significant as compared to non-pregnant women group, which then was increased in the second trimesters, and declined in the third trimester than the mean of non-pregnant women. The mean FT4 levels in the first and the second trimesters were non-significantly lower than that of the non-pregnant subjects. But in the third trimester, the mean FT4 significantly decreased than the mean for non-pregnant women. Mean FT3 values showed declining over the trimesters relative to the non-pregnant control group that were significant in second and third trimesters. In each trimester, the mean TSH levels of pregnant women were lower than the mean level of non-pregnant but were not statistically significant in second and third trimesters.

Table 2: Thyroid status in pregnant and non-pregnant women (mean ± SD)

Parameters	TT4	TT3	FT4	FT3	TSH
Non-pregnant women (n=75)	87.42 ± 30.11	2.83 ± 1.27	14.96 ± 6.21	6.38 ± 2.98	2.68 ± 1.11
Pregnant women (n=75)					
First trimester (n=25)	79.22 ± 38.42 ^{NS}	2.91 ± 1.12^{NS}	14.81 ± 4.11 ^{NS}	6.91 ± 2.63 ^{NS}	1.87 ± 1.02 **
Second trimester (n=25)	91.76 ± 40.33 ^{NS}	3.42 ± 1.25*	12.56 ± 3.96 ^{NS}	4.79 ± 2.10 **	2.22 ± 1.19 ^{NS}
Third trimester (n=25)	122.18 ± 49.32 ***	2.95 ± 1.43^{NS}	9.54 ± 4.12 ***	3.72 ± 1.33 ***	2.49 ± 0.94 ^{NS}
Overall	102.17 ± 40.11 **	3.31 ± 1.30 **	11.78 ± 4.48 ***	5.09 ± 2.02**	2.15 ± 1.03 **

Pregnant subjects compared with non- pregnant subjects (* p<0.05, ** p<0.01, ***p<0.001), NS - Not significant

DISCUSSION

This study was planned to document the gestational associated changes in thyroid related hormones with respect to nonpregnant women residing in the same area. Compared to nonpregnant women, the relatively low TSH in pregnant women during the first trimester was due to TSH suppression in 14% of them. This early pregnancy TSH suppression is attributed to extremely high concentration of hCG that has TSH-like activity [15] and inhibits thyrotropin-releasing hormone (TRH) secretion [16]. It is plausible as both TSH and hCG are heterodimeric glycoproteins composed of a common α-subunit, and they share considerable similarity in their ß-subunits with similar receptors [1]. This additional stimulation of thyroid gland diminishes during the second and the third trimesters [15, 17]. The increase in TSH levels during pregnancy is reported in many studies [18–22]. Panesar NS *et al*. Performed a study with 343 healthy pregnant women (5-41 weeks) and 63 non-pregnant controls to establish gestation-related reference intervals for thyroid hormones in pregnant Chinese women [9]. The study reveled that FT3 decreased during pregnancy, whereas FT4 initially increased, peaking between 9-13 weeks and then decreased, the decline becoming significant by week 21, and TSH changes was similar to FT4. We also found declining in FT3 over the pregnancy. FT4 changes during pregnancy in our studywas decreased in third trimister. In contrast to Panesar *et al*. [9], we did not find a significant change in the mean TSH level in the second and third trimesters, but in the first trimester, the mean TSH level of pregnant women was significantly lower than that of non-pregnant women.

McElduff found that the FT4 decreased during pregnancy compared to non-pregnant women, and this resulted in the need for each laboratory to develop its own reference range for FT4 levels in pregnancy [11]. Erem *et al*. investigated maternal thyroid function in 29 pregnant women with goiter and 51 pregnant women without goiter. The location of the women was the eastern black sea region of Turkey, which is an endemic goiter area [13]. It was found that TT4, FT4, TT3, FT3, and thyroxine binding globulin increased during pregnancy. They also found that serum TSH levels declined in pregnant women without goiter compared with non-pregnant women without goiter. In our study, changes in the serum levels of TT4 & TT3 in pregnant women were closely similar to those reported by Erem *et al*. [13].

But in contrast to their findings, we found that serum levels of FT4, FT3 & TSH in pregnant women decreased compared to those of non-pregnant women. The etiology of increase in total circulating thyroid hormones primarily involves increased concentrations of plasma thyroxine binding globulinduring pregnancy [5]. Another proposed mechanism for the increased total thyroid hormone concentrations is production of type III deiodinase by the placenta. This enzyme, which converts T4 to reverse T3, and T3 to diiodotyrosine (T2), has extremely high activity during fetal life. Increased demand for T4 and T3 has been suggested to increase production of these hormones which ultimately increases the circulating concentrations of the hormones [5]. Increased sialylation, mediated by oestrogens, reduces the heptic clearance of thyroxine binding globulin, resulting in increased levels of both TT4 and TT3 [9]. Changes in albumin and free fatty acid concentrations sustain the binding of T4 and T3 to carrier proteins; this lowers the blood levels of FT4 and FT3 as pregnancy progresses [8, 9].

CONCLUSION

It is important that thyroid function tests in pregnancy should be interpreted against gestational age-related reference intervals, and the result of this study could decline the possibility of the misinterpretation of thyroid function in pregnant women. The availability of gestational age-dependent reference intervals for thyroid hormones for local population should help to avoid the under diagnosis of hyperthyroidism or the over diagnosis of hypothyroidism. It also allows an accurate interpretation of thyroid hormone results in complicated pregnancies. In summary, we found the evidence to support the hypothesis that, during pregnancy, thyroid function adapt in a physiological way to meet the increased demands for iodine and energy.

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