Thyroid Hormone Status of Normal Pregnant Women

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Research Article

Abstract: **Objectives:** To study thyroid hormone status of normal pregnant women in each trimester and compare it with non-pregnant women. **Materials and Methods:** This was a longitudinal type of study. Serum levels of T3, T4 and TSH were estimated by ELISA technique in normal pregnant women (n=60) in each trimester and compared with age matched control (n=60). **Results:** We found significant increase in T3 and T4 level in 1st trimester (P<0.01) when compared to control group. In 2nd trimester values increased further (P<0.01) and in 3rd trimester increase was statistically highly significant (P<0.001). We observed decreased TSH level in 1st trimester (P<0.01) when compared to control group. In 2nd trimester values increased further but difference was not statistically significant (P>0.05). In 3rd trimester there was statistically significant rise in values when compared to control group. **Conclusion:** Interpretation of thyroid function test in pregnancy needs care and separate reference intervals should be used.

Key words: Thyroid, Normal pregnancy.

Introduction

In any community, mothers and children constitute a priority group. They not only constitute a large group, but also a "vulnerable" or "special risk" group. The risk is concerned with child bearing in case of women[1]. Pregnancy denotes one of the most important states of physiological adaptation in human body[2]. Endocrine glands play very important role in physiology of reproduction, one of the important system is thyroid gland[3]. Thyroid hormones interfere with numerous aspects of reproduction such as disturbed ovarian function and can adversely affect pregnancy outcome. Thyroid hormones are important in development of brain and neurological outcome of fetus.Thyroid hormones appear to have their most profound effects on the terminal stages of brain differentiation, including synaptogenesis, growth of dendrites and axons, myelination and neuronal migration. Thyroid hormone receptors are present prior to the time, fetus is able to synthesize thyroid hormone[4]. Thyroid disorders are observed four to five fold more frequently in women of child bearing age when compared to men[5].Normal thyroid function is important to maintain normal reproduction via its interaction in several pathways[6]. The thyroid dysfunction particularly hypothoroidism is common in gestation[7]. In this longitudinal study, the status of maternal thyroid gland is studied by thyroid function tests (T_3, T_4, TSH) in all the three trimesters of pregnancy and the changes which occurred in order to meet increased demands during pregnancy are observed.

Aims and Objectives

Recognition of abnormality in thyroid function tests during pregnancy is important for the welfare of mother as well as fetus. The values of T_3, T_4, TSH in non pregnant women are not applicable during pregnancy[8]. There have been few attempts to make a serial estimation of physiological changes produced by pregnancy on various systems. Also there is no unanimous opinion regarding the various changes in thyroid function tests during pregnancy. In the present study, we attempt to clarify the functional activity of maternal thyroid throughout pregnancy. One of the aims of present study is to underscore the rationale that allows for a correct interpretation of the alterations in thyroid hormone levels. Another aim is to discuss the specific role attributed to each factor and delineates the main pathways of thyroidal adaptations in pregnancy state.

Objectives of the study are;

a. To find out thyroid hormone status of normal pregnant women in each trimester.
b. To compare serum thyroid hormonal level in normal pregnant women as compared to non-pregnant women.

Materials and Methods

A longitudinal study was conducted on 60 normal pregnant women attending antenatal care outpatient department for regular check-up in the Department of Obstetrics and Gynaecology, Government Medical College & Hospital, Nagpur. Protocol of study had first been accepted by Ethical Committee. Informed consent was obtained from each subject. At initial evaluation, a detailed history of past gynaecological

events was obtained. A detailed history of thyroid related past events was also recorded. Each subject was examined for presence of thyroid enlargement or other signs of thyroid disease. Inclusion and exclusion criteria for subjects are given below.

Inclusion Criteria

1. Age : 18 – 30 years
2. Apparently normal, healthy, primigravida attending ANC Clinic at GMC, Nagpur.
3. With known date of last menstrual period.
4. Ready to attend ANC Clinic regularly till delivery.

Exclusion Criteria

1. History of thyroid disease or therapy, having palpable goiter or with evidence of thyroid abnormality.
2. Diabetes mellitus, hypertension or other metabolic disorders, cardiac disease, carcinoma, infection.

Age matched 60 non-pregnant healthy women with reliably known clinical history formed a Control group. Three serial blood samples were collected from each pregnant woman once in each trimester. Average period of sample withdrawal was for 1st trimester 8-10 weeks, 2nd trimester 18-20 weeks, 3rd trimester 32-35 weeks. An effort was made to obtain a sample early in pregnancy and for this purpose, patients who came for pregnancy confirmation in Gynaecological OPD after single missed period were included. Before withdrawing blood, gestational age was calculated from last menstrual period and uterine size.Approximately 3 ml fasting blood sample was collected by observing due norms from each subject and control. Total T_3, Total T_4 and TSH were estimated by ELISA method in the Department of Biochemistry, Government Medical College, Nagpur.

Dropouts

1. Two subjects were excluded from the study that could not complete gestation because of miscarriage.
2. One subject could not be followed up.
3. One subject was diagnosed as hypothyroid after first sample evaluation.

All dropouts were replaced by other subjects in due course of time.

Statistical Analysis

Results were expressed as mean ± SD. Statistical analysis of data was performed using one way analysis of variance (ANOVA) followed by Tukey's post-hoc test. Two tailed P values were used throughout and the P value less than 0.05 were judged statistically significant. Statistical calculations were done by using Graph Pad Prism, Version 3.02.

Observations and Results

The biochemical parameters of thyroid function, expressed as mean values per trimester of gestation are given in tables.

Table 1: Total triiodothyronine levels in three trimesters of pregnancy

Group	T3 (ng/ml)	P value
Control	0.962 ±0.116	
First trimester	1.283 ± 0.257	P<0.01
Second trimester	1.437 ± 0.18	P<0.01
Third trimester	1.499 ± 0.149	P<0.001
One way ANOVA	F= 102.4	P<0.001

Values are mean ± SD, n(Number of subjects or controls) 60 in each group ; df=3,236 one way ANOVA followed by tukey's post hoc test

Mean values of total triiodothyronine levels in three trimesters of pregnancy are shown in table 1. We found significant increase in T3 level in first trimester, when compared to control group (P<0.01). In second trimester, values increased further (P<0.01) by 12%. In third trimester, increase was statistically highly significant (P<0.001). Thus we observed a rising trend of T3 levels throughout pregnancy.

Table 2: Total Thyroxine Levels in Three Trimesters of Pregnancy

Group	T4(µg/dl)	P value
Control	7.828 ±2.222	
First trimester	10.28 ± 0.841	P<0.01
Second trimester	10.59 ± 0.809	P<0.01
Third trimester	10.95 ± 0.642	P<0.001
One way ANOVA	F=71.79	P<0.001

Values are mean ± SD, n = 60 in each group ; df=3,236 one way ANOVA followed by Tukey's post hoc test.

Table 2 shows mean values of total thyroxine levels in control as well as in study groups. Levels of T4 increased in first trimester, when compared to control group (P<0.01). In second and third trimester, there was significant (P<0.01) and highly significant (P<0.001) increase observed respectively. Sharp rise in T4 level was observed in 1st trimester, followed by gradual rise in second and third trimester.

Table 3: Thyroid stimulating hormone levels in three trimesters of pregnancy

Group	TSH (µIU/ml)	P value
Control	1.843 ±0.655	
First trimester	1.296 ± 0.467	P<0.01
Second trimester	1.913 ± 0.684	P>0.05
Third trimester	2.177 ± 0.894	P<0.05
One way ANOVA	F =17.13	P<0.001

Values are mean ± SD, n = 60 in each group ; df=3,236 one way ANOVA followed by Tukey's post hoc test

Mean values of TSH levels in control and study groups are shown in table 3. We observed, decreased TSH value in first trimester of pregnancy, when compared to control group (P<0.01). In second trimester,

values increased above control values by 4% and the difference was statistically insignificant. In third trimester, we observed a statistically significant rise in values, when compared to controls ($P<0.05$). After initial decrease in first trimester, TSH value approaches control value in 2nd trimester and peaks at third trimester.

Discussion

Pregnancy constitutes a unique experimental model in humans, wherein normal thyroid is faced with multiple challenges. To meet the challenge of increased needs during pregnancy thyroid adapts through changes in thyroid hormone economy and regulation of hypothalamic pituitary thyroid axis[9]. In the present study, we have attempted to define the changes in maternal thyroid hormones in women without detectable thyroid abnormalities and clarify their physiological significance. The study differs from previous studies on thyroid hormone levels in normal pregnancy, primarily with respect to sample size, follow up of same subject during each trimester throughout pregnancy and geographical area. In the present study, we observed a rising trend of T_3 level throughout pregnancy. These findings are in correlation with previous studies by and **Glinoer D et al**[9] **Lazarus JH**[10]and **Ballabio M et al**[11]. In the present study, we observed levels of T_4 increased in first trimester when compared to Control. In second and third trimester, there was significant rise observed. These findings are supported by **Guillaume et al**[12] , **Burrow GN et al**[3] and **Lazarus JH**[10] . Similarly higher values were observed by **Elahi S et al**[13], **Kandakar MA et al**[14]. It is probable that the changes in thyroid hormone during gestation relate to necessity of delivering thyroxine to the foetal cells,particularly neuronal cells[10]. The etiology of this increase in total circulating thyroid hormones (T_3 and T_4) involved primarily increased concentration of plasma thyroxine binding globulin, production of Type II deiodinase from placenta[15] and increased demand leading to glands increased hormonal output[16]. . Due to their increased serum concentration it has been teachnically easier to develop assay for total thyroid hormones and these are more accurate and valid than free hormone assay. In our study, we observed that in first trimester of pregnancy, level of TSH was decreased below control value of non pregnant women and this difference was statistically significant. Our findings are in correlation with the study of **Guillaume J et al**[12], **Pekomen et al**[17], **Yoshikawa N**[18] and **Krassas G E et al** [19].In second trimester, values of serum TSH increased above control values by 4% and difference was statistically insignificant, while values were significantly increased in third trimester. These findings are coexistent with studies by **Glinoer D et al**[9], **Kumar A et al**[8]. Decreased TSH level during 1st trimester could be due to partial suppression of TSH due to elevation of circulating hCG level which has thyrotropic action due to structural homology between hCG and TSH molecules[6,19]. Increase in TSH during late gestation, generally remaining within reference range may reflect a stimulated thyroid state.

Conclusion

It is clear from the study that the interpretation of thyroid function tests in pregnancy needs care and separate reference intervals should be used.

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