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# Study of Thyroid-Related Hormones During Second Trimester of Pregnancy

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**A study during second trimester of pregnancy was conducted among 100 women from a population with mild to moderate deficient iodine intake (median 7 μg/L) to monitor the changes in serum free thyroxin ($FT_4$), triiodothyionine ($T_3$) and thyrtropin (TSH). Thyroid related hormones were assessed using radioimmunoassay (RIA) and immunoradiometricassay (IRMA).**

**As compared with non pregnant women, mean $FT_4$ levels decreased, $T_3$ levels increased and TSH levels were slightly depressed in pregnant women. Mean $FT_4$ concentration reached its highest level in the 4th month and linearly decreased until the 6th month. Mean $T_3$ level remained almost constant during 2nd trimester of pregnancy. Mean TSH level remained unaltered during the 4th and 5th months and was slightly lower than that for the control group. However, these differences were statistically insignificant. At the end of the second trimester, hypothyroxinemia and $T_3$ levels greater than the upper limit of the laboratory reference range were found in 34% and 38% of women, respectively. These changes in thyroid hormones reflect typical adaptations of the thyroid gland during pregnancy to the limited availability of iodine.**

**Key words** : Iodine deficiency, Pregnancy, Pakistan

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## INTRODUCTION

Pregnancy causes changes in the anatomy and function of the thyroid gland because of the increased demand of thyroid hormones throughout gestation.[1)] Pregnancy results in an elevation of the serum concentration of thyroid-binding globulin (TBG), direct stimulation of the thyroid gland owing to elevated levels of human chorionic gonadotropin (hCG), which may transiently decrease serum TSH, and increased enzymatic activity of type III monodeiodinase, which coverts $T_4$ to $T_3$ in the placenta.[1,2)] The thyroid gland has to adapt in a physiological way to the increased demand of thyroid hormones. Successful thyroid adaptation depends on the intact functional capacity of the thyroid gland and the adequate availability of dietary iodine.[1-3)]

Iodine is essential for the synthesis of thyroid hormones. During pregnancy, maternal iodine requirements are enhanced due to the increased renal clearance of iodine and the diversion of a portion of maternal iodine to the fetus for thyroid hormones synthesis by the fetal thyroid gland during the second trimester.[1-3)] These factors are particularly important in areas where maternal iodine intake is low because increased renal clearance of iodine gears up in the early weeks of pregnancy and persists until parturition.[4,5)] Consequently, iodine deprivation during the first trimester is markedly aggravated in the later part of pregnancy and the production of thyroid hormones is compromised.[4,5)] The typical pattern in iodine-deficient areas is the relative hypothyroxinemia (a conditioned characterized by low free $T_4$ and normal TSH), preferential $T_3$ secretion and enhanced TSH level, relative to the degree of iodine deficiency.[1-5)]

An optimum level of thyroid hormones is essential for the normal development of the brain and nervous system of the fetus.[6,7)] Iodine deficiency disorders (IDD) are a major nutritional problem in Pakistan, affecting up to 15 million people.[8)] The typical Pakistani diet contains low iodine content (average 40 μg/day)[9)] and it is estimated that 30% of households in Pakistan consume iodized salt.[10)] Pregnant women suffer from iodine depletion due to closely spaced and repeated pregnancies.[11)] The incidence of goiter (the most visible IDD) among pregnant and lactating women has been reported as 0.1%.[12)]

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Previous studies[13,14] have reported a prevalence of mild to moderate iodine deficiency in pregnant women in Lahore, with a median urinary iodine excretion level of 70 μg/L during the first trimester of pregnancy.[14] The present study is an attempt to assess the level of serum $FT_4$, $T_3$ and TSH as influenced by the advancement of gestation in an iodine-restricted environment.

## MATERIALS AND METHODS

### 1. Subjects

The study was conducted from March to October 2004. One hundred pregnant women (n=100) in the second trimester of pregnancy were interviewed and selected from the department of obstetrics and gynecology at the government-run Mian Muhammad Munshi hospital, in Lahore. All of them were visiting for antenatal checkups. Purpose of the study was explained to each woman and their past reproductive histories were recorded in detail. Women who had suffered from thyroid disease, were on medication or had been through surgery were not included in this study. Fetal age was confirmed by ultrasonography performed at the same hospital. For the sake of comparison, 100 normal, non-pregnant women having no goiter and comparable parity were also placed under study as control subjects. As far as iodine nutrition is concerned, there was no change in the routine diet with the onset of pregnancy.

### 2. Blood Collection

The first blood sample was drawn, on average, in the 14th week of gestation. The second and third blood samples for the same women were drawn at one-month intervals (average was between 18 and 23 weeks of gestation). Five milliliters of blood were taken in a disposable syringe and refrigerated. Serum was separated using low speed centrifugation (2000x g) at room temperature and the serum samples were stored at −20℃ until analysis for $FT_4$, $T_3$ and TSH.

### 3. Analytical Procedure

$FT_4$ and $T_3$ were estimated using radioimmunoassay (RIA) and TSH was estimated using immunoradiometric assay (IRMA) as described by Abbas *et al.*.[15] The assay reliability of IRMA and RIA was determined through the use of commercially derived control sera of low, medium and high concentrations of thyroid-related hormones, which were included in every run. All assays were carried out in duplicate. Precision profile showed inter- and intra- assay coefficients of variation (CV) of less than 10% over the entire measurement range for TSH and both thyroid hormones and samples showing more than 10% CV were reanalyzed. Measurement of radioactivity, the fitting of the standard curve and the analysis of samples was carried out using a computerized gamma counter (Cap-RIA 16, CAPINTEC Inc, USA). Reference laboratory ranges for $FT_4$, $T_3$ and TSH were 11.0-22.0 pmol/L, 1.10-3.0 nmol/L and 0.35-4.0 mIU/L, respectively.

### 4. Statistical Analysis

Various descriptive statistics (mean, standard deviation, range) and analysis of variance were computed for the data[16] using SPSS software (SPSS Inc., Chicago, USA) on a personal computer.

## RESULTS

The characteristics of the study and control women are given in Table 1. Both groups had similar parity, incidence of past abortions and number of living children. The ages of pregnant women ranged from 15-40 years (mean±SD 24.0±4.2 years). The control women were slightly older than the pregnant women. However, the difference was not significant.

**Table 1.** Characteristics of the study and control women (n=100)

| Parameters | Study subjects | Control |
|---|---|---|
| Age (years) | 24.0±4.2 | 26.0±5.6 |
| Parity (average) | 3.1±2.1 | 3.2±2.3 |
| Incidence of Abortion (%) | 34 | 30 |
| Mean alive Children | 2.4 | 2.8 |
| Goiter | None | None |

The results of the study are summarized in Table 2, which shows the overall trend of the changes in thyroid hormone parameters during second trimester of pregnancy. As compared to the control subjects, mean $FT_4$ levels in each month of the pregnancy. As compared to the control subjects, mean $FT_4$ levels in each month of the second were significantly lower ($p<0.05$). However, within the trimester they remained almost constant. In contrast, $T_3$ levels in the pregnant women were significantly ($p<0.05$) higher as compared to those of the non-pregnant women. The mean $T_3$ level almost doubled in pregnant women as compared to that for the control group. In the 6th month, 38% the women had $T_3$ levels

**Table 2.** Variation in thyroid related hormones during second trimester of pregnancy (Mean±SD)

| Hormone[1)] | Month of pregnancy | | | Control | Normal[2)] (Range) |
|---|---|---|---|---|---|
| | 4th | 5th | 6th | | |
| $FT_4$ (pmol/L) | 13.2±3.4[a] (9.1-23.9) | 12.2±3.2[a] (9.4 - 23.0) | 12.4±3.1[a] (8.3 - 20.2) | 16.1±3.9[b] (9.6 - 32.1) | 11.0-22.0 |
| $T_3$ (nmol/L) | 2.9±0.6[a] (1.2-4.0) | 2.9±0.5[a] (2.1-4.8) | 2.9±0.5[a] (2.6 - 4.8) | 1.6±0.4[b] (0.8 - 2.9) | 1.10-3.00 |
| TSH (mIU/L) | 1.2±0.9[a] (0.05-2.9) | 1.2±0.7[a] (0.05-3.9) | 1.3±0.7[a] (0.3 - 3.9) | 1.5±1.0[a] (0.1 - 6.1) | 0.35-4.0 |

1) $FT_4$: free thyroxine; $T_3$: triiodothyronine; TSH: thyrotropin,
2) Values used as normal at the Centre for Nuclear Medicine, Mayo Hospital, Lahore, Pakistan.
Value in parenthesis indicates min-max values (Range).
Means within a row followed by different letters are significantly different at $p<0.05$.

greater than the upper limit of our laboratory reference range (Table 2). TSH values observed through out the second trimester were lower than those for the control group but the difference was not statistically significant. Mean TSH levels remained the same in 4th and 5th month and rose slightly in the 6th month. However, variation within the trimester was insignificant. None of the pregnant women had TSH level greater than the upper limit of our laboratory range. It was observed that five pregnant women in the 4th month and one in the 5th month and had undetectable levels of TSH in serum. None of the women in the control group had undetectable levels of TSH in serum. During the 6th month of pregnancy, none of the women in the study sample had undetectable levels of TSH. The number of hypothyroxinemic women in the 4th month was 32%, which increased to 34% in the 5th month and then remained stable.

## DISCUSSION

The objective of the study was to investigate the dynamics of changes in thyroid-related hormones with the progression of gestation in women with low iodine intakes. The prevalence of hypothyroxinemia and elevated $T_3$ secretion in about one-third of the pregnant women indicates marginal dietary iodine intake. However, it was not severe enough to induce excessive thyroid stimulation.[4,5,17)] TSH levels in most of the women remained within the normal reference range. Lower mean levels of TSH in pregnant women were the result of undetectable TSH levels (0.05 mIU/L) in a number of them. This transient suppression of TSH may be due to elevated hCG levels.[2,18)] Such a phenomenon has been observed early in pregnancy.[2)] Our results suggest that observed suppression is not restricted to the first trimester and continues even in the 4th and 5th months.

The high incidence of maternal hypothyroxinemia during the first half of the pregnancy is alarming. It is blamed for the deficient neuro-intellectual development of fetuses.[19,20)] In early pregnancy, maternal hypothyroxinemia can negatively effect the differentiation, growth and development of the fetal brain.[6)] Iodine deficiency also contributes to the occurrence of hypothyroidism in pregnant women, which may affect the outcome of the pregnancy and result in gestational complications.[21-23)]

The results of the present study are in line with those of UNICEF, according to which 81% of the population in Punjab is iodine deficient.[24)] The restricted level of iodine intake is presumably sufficient to cover the usual needs of thyroid hormone production in normal adult subjects because goiter is not endemic. However, it is inadequate to meet the extra requirements when physiological conditions such as pregnancy intervene. Our results confirm the fact that pregnancy acts as an indicator of the underlying iodine restriction by its increased hormonal demands and obligatory iodine losses. Consequently, it results in a relative iodine-deficient state.[2,17)]

In the light of foregoing discussion, it may be postulated that the physiological changes associated with pregnancy in an iodine-restricted environment may result in profound maternal thyroid stress and hypothyroxinemia, which may trigger maternal thyroid pathology and deficient nervous system development in the fetus. The results of this study indicate that about one-third of pregnant women and their fetuses may be at risk. This study provides a rationale for iodine supplementation.

## Literature Cited

1) Glinoer D. What happens to the normal thyroid during pregnancy? *Thyroid* 9:631-635, 1999
2) Glinoer D. The regulation of thyroid function in pregnancy: pathways of endocrine adaptation from physiology. *Endocr Rev* 18:404-33, 1997
3) Mezosi E, Molnar I, Jakab A, Balogh E, Karanyi Z, Pakozdy Z, Nagy P, Gyory F, Szabo J, Bajnok L, Leovey A, Kakuk G, Nagy A. Prevalence of iodine deficiency and goiter during pregnancy in east Hungry. E.V. *Eur J Endocrinol* 143: 479-83, 2000
4) Caron P, Hoff M, Bassi S, Dufor A, Faure G, Ghandour I,

Lausu P, Lucas Y, Maraval D, Mignot F, Ressigeac P, Vertongen F, Grange V. Urinary iodine excretion during normal pregnancy in healthy women living in the Southwest of France: correlation with maternal thyroid parameter. *Thyroid* 7:749-754, 1997

5) Vermiglio F, Lo-Presti VP, Castagna MG, Visli MA, Moleti M, Finocchiaro MD, Mattina F, Artemisia A, Trimarchi F. Increased maternal thyroid failure with pregnancy progression in an iodine deficient area with major iodine deficiency disorders. *Thyroid* 9:19-24, 1999
6) Bernal J, Guadano-Ferraz A, Morte B. Perspectives in the study of thyroid hormone action on brain development and function. *Thyroid* 13:1005-1012, 2003
7) Auso E, Lavado-Autric R, Cuevas E, Escobar del Rey F, Morreale de Escobar G, Berbel P. A moderate and transient deficiency of maternal thyroid function at the beginning of fetal neocorticogenesis alters neuronal migration. *Endocrinology* 145:4037-4047, 2004
8) UNICEF. Iodine Deficiency Disorders (IDD). *Medical Herald (special supplement)* 18:11-14, 2001
9) Akhter P, ur-Rehman K, Orfi SD, Ahmad N. Assessment of iodine levels in the Pakistani diet. *Nutrition* 20:783-787, 2004
10) Goverment of Pakistan. National Nutrition Survey 2001-2002. Planning Commission. Islamabad, 2003
11) Government of Pakistan. Life cycle approach to women's health. In: Pakistan reproductive health service package. pp.5, Ministry of health and population welfare. Islamabad, 1999
12) Government of Pakistan. National Nutrition Survey Report. National Institute of Health, Islamabad, 1998
13) Elahi S, Syed Z, Nagra SA. Status of iodine deficiency disorders as estimated by neonatal cord serum thyrotrophin in Lahore, Pakistan. *Nutr Res* 24:1005-10, 2004
14) Fareeha R. Iodine intake and thyroid related hormones during first trimester of pregnancy. M. Sc. Thesis. Institute of Chemistry, University of the Punjab, Lahore. 2002
15) Abbas HG, Elahi S, Khan MS, Naeem M. Serum thyroxine ($T_4$) and thyroid stimulating hormone (TSH) levels in cord blood of newborns in Lahore. *Pak J Med Sci* 19:211-216, 2003
16) Sneedecor GW, Cochran WG. Statistical Methods. Iowa State University Press, 1976
17) Glinoer D, DeNayer P, Bourdoux P, Lemone M, Robyn C, Van Steirteghem A. Regulation of maternal thyroid during pregnancy. *J Clin Endocrinol Metab* 71:276-287, 1990
18) Yoshimura M, Hershman JM. Thyrotrophic action of human chorionic gonadotropin. *Thyroid* 5:425-434, 1995
19) Pop VJ, Kuipens J, Van L, Barr AL. Low normal maternal free $T_4$ concentrations during early pregnancy are associated with impaired psychomotor development in infancy. *Clin Endocrinol* 50:149-155, 1999
20) Calvo RM, Jauniaux E, Gulbis B, Asunción M, Gervy C, Contempré B, Morreale de Escobar G. Fetal tissues are exposed to biologically relevant free thyroxine concentrations during early phases of development. Possible consequences of maternal hypothyroxinemia. *J Clin Endocrinol Metab* 87:1768-1777, 2002
21) Dillon JC, Milliez J. Reproductive failure in women living in iodine deficient areas of West Africa. *Br J Obstet Gynocol* 107:631-636, 2000
22) Glinoer D. The systematic screening and management of hypothyroidism and hyperthyroidism during pregnancy. *Trends Endocrinol Metab* 10:403-411, 1998
23) Dunn JT, Delange F. Damaged reproduction: The most important consequence of iodine deficiency. *J Clin Endocrinol Metab* 86:2360-2363, 2001
24) UNICEF. Punjab: socio-economic profile. In: A better future for children and women in Pakistan, pp.1-13, Lahore, 1995