*Original Article*

# Assessment of Thyroid Function During the Three Trimesters of Pregnancy.

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## Abstract:

**Background:** Undetected and untreated thyroid disorders are associated with adverse maternal and fetal outcomes. There are limited data on the prevalence of newly diagnosed thyroid disease during pregnancy from Egypt Therefore; this study was designed to evaluate the prevalence of thyroid dysfunction during the three trimesters of pregnancy. Pregnancy is associated with significant but reversible changes in thyroid function due to the effect of HCG and estrogen. That might cause maternal and fetal complications so screening is important. **Patient and Method:** The present cross-sectional study was conducted at antenatal clinic of El Chatby Maternity Hospital in Alexandria University. The total sample population comprised of of 90 pregnant women divided into 30 women for each trimester compared with 30 non pregnant healthy women regarding thyroid function parameters and anti-TPO by using COBAS analyzer measured by the electrochemiluminescence immunoassay "ECLIA" employs monoclonal antibodies specifically directed against human TSH,FT4,FT3 and anti TPO. **Results:** 120 ladies were enrolled for this study aged between 20-45years excluding ladies with previous endocrinal anomalies showed significant difference between pregnant and non- pregnant females regarding TSH and FT4 and no significant difference regarding FT3 and anti TPO in all trimesters. **Conclusion:** There is discrepancy between FT4 &TSH in pregnancy due to presence of other stimulatory and inhibitory factors in pregnancy and thyroid anomalies increased with advance in pregnancy so screening of TSH and anti TPO is important. Considering the immense impact that maternal thyroid dysfunction has on maternal and fetal outcomes, prompt identification of thyroid dysfunction and its timely treatment is essential.

**Keywords:** Thyroid function, Trimesters, Pregnancy.

## Introduction:

The thyroid gland is one of the largest endocrine glands in the body, weighing 2-3 grams in neonates and 18-60 grams in adults, and is increased in pregnancy. This gland is found in the neck inferior to the thyroid cartilage, produces the hormones T4, T3, and calcitonin. Up to 80% of the T4 is converted to T3 by peripheral organs such as the liver, kidney and spleen. T3 is about ten times more active than T4. It plays a vital role in the overall body function during all stages of life; it produces hormones that regulate the body's overall metabolism, the rate at which the body produces energy from nutrients. Pregnancy is associated with significant but reversible changes in thyroid function. These are a result of normal physiologic state and hormonal changes that alter thyroid function.[1] Therefore, some experts strongly recommend universal screening either before conception or at least when pregnancy is confirmed. [2]The high circulating estrogen levels during pregnancy change the pattern of glycosylation of TBG at the time of hepatic synthesis, leading to a longer plasma half-life and, consequently, an increase in the plasma TBG concentration[3] This lead to increased serum T4 -binding globulin and T4 concentrations.[4,5]

Although a transient decrease in serum free T4, followed by a rise in TSH to a new equilibrium, may occur,[6] this is usually not appreciated with routine thyroid testing. A high

circulating HCG level in the first trimester leads to HCG cross reactivity with the TSH receptor, prompting a temporary increase in free T4 and partial suppression of TSH. The final physiologic change results from placental deiodination of maternal T4, which increases T4 turnover. Fetal thyroid function begins from the end of the first trimester. Prior to that, there is evidence that normal development of the fetal brain is dependent upon maternally derived T4, which is converted intracellular to T3. Such T4 has been detected from 5-8 weeks' gestation and by 11 weeks it is at 100 time greater concentration than in the maternal circulation. Maternal hyothyroxinaemia at this stage may have adverse effects on subsequent fetal brain development. Fetal FT4 and total T4 reach adult levels by 36 weeks gestation. Fetal TSH is greater than adult TSH and fetal T3 remains low. The relatively high levels of T4 allow intracellular conversion to T3 in the fetal brain. The aim of this work was to assess thyroid functions in a group of pregnant women attending the Pregnancy Outpatient Clinic at the Chatby Maternity Hospital in Alexandria University, and to compare the results with matching non-pregnant women.

**Patients and Methods:**

The present cross-sectional study was conducted at antenatal clinic Department of the Obstetrics and Gynecology. The total sample population comprised of 90 pregnant ladies of the three trimesters of gestation without any history of thyroid disease or intake of any thyroid medication and 30non-pregnant healthy ladies as control. On the enrollment of participants, an informed written consent was taken, detailed history was enquired, participants were subjected to relevant general physical examination and findings were recorded on a predesigned preform. 3 mL blood was sampled from the participants under aseptic conditions; stable for 7 days at 2-8 °C, 1 month at -20 °, they were frozen only once, the sample types listed were tested with a selection of sample collection tubes, and we centrifuged samples containing precipitates before performing the assay heat-inactivated samples do not used. The samples, calibrators, and controls were at ambient temperature (20-25 °C) before measurement. They were analyzed for thyroid function tests, which included FT3, FT4, TSH and anti-thyroid peroxidase antibodies (TPO) by using the electrochemiluminescence technique. The analyzer was Cobas with immunoassay analyzer The Eleusis TSH assay employs monoclonal antibodies specifically directed against human TSH. The antibodies labeled with ruthenium complex consist of a chimeric construct from human and mouse-specific components. As a result, interfering effects due to HAMA (human anti-mouse antibodies) are largely eliminate also FT4 and FT3 was measured by the same principle through Competition principle: 1st incubation: 15 µL of sample and a T3 or T4-specific antibody labeled with a ruthenium compel,. 2nd incubation: After addition of biotinylated T4 and streptavidin-coated 2microparticles, the still-free binding sites of the labeled antibody become occupied, with formation of an antibody-hapten complex. The entire complex becomes bound to the solid phase via interaction of biotin and streptavidin. The reaction mixture is aspirated into the measuring cell where the micro particles are magnetically captured onto the surface of the electrode. Unbound substances are then removed with Propel/Propel M. Application of a voltage to the electrode then induces chemiluminescent emission which is measured by a photomultiplier. Results were determined via a calibration curve which is instrument-specifically generated by 2-point calibration and a master curve provided via the reagent barcode. Regarding anti TPO the Elecsys Anti-TPO Cal Check calibration verification solutions comprise three levels - low, mid and high - each with a defined Anti-TPO concentration. The low solution concentration is near the lower detection limit of the assay. The mid solution is in the middle or at a clinically critical point of the measuring range. The high solution is near the upper limit of the measuring range.

## Results:

A total of 120 women were enrolled for this study: 30 ladies in each trimester of the three trimesters and 30 non- pregnant healthy ladies as a control, from El Chatby Alexandria university hospital. The mean age among ladies in 1$^{st}$ trimester was 26.10 years, in

2nd trimester was 27.33 years, and in 3rd trimester was 27.83 years and in non- pregnant ladies was 27.37 years. No significant difference between the ages in the four groups. Regarding thyroid dysfunction symptoms; all cases of thyroid disorders were asymptomatic compared to 3cases in non-pregnant women having palpitation, hair loss and menses disturbance (10%). This referred to the magnitude of the problem that most cases of thyroid disorders were asymptomatic and if there were symptoms these were closely similar to physiological symptoms of pregnancy so screening is important. By examination of the ladies 3 women in pregnant women group were have goitre (3.3%): 2 women were found with goiter (by examination) in 3rd trimester and 1 woman in 2nd trimester.The study showed significant difference between pregnant women and non-pregnant control group according to mean of TSH and FT4 but it showed no significant difference between pregnant women and non-pregnant control group regarding FT3 and anti TPO (Table I & II).

Regarding anti TPO, it showed significant difference between 3rd trimester and non-pregnant control group, no significant difference between 2nd trimester and non-pregnant control group and there was no significant difference between 1st trimester and non-pregnant control group however; it shows no significant different between pregnant and non-pregnant ladies.

Euthyroid state was in 76.7 % of pregnant in 1st trimester compared to control 73.3% with least percentage in 3rd trimester 46.7%, hypothyroidism was more prevalent in 3rd trimester that was 40% and that associated with Anti TPO in 13.3%, subclinical hypothyroidism is more prevalent at 1st trimester 10% of women compared to control women which is 6.7% and that associated with anti TPO prevalent in 1st trimester 6.7% of women. Hyperthyroidism is more prevalent in 3rd trimester 10% compared to non-pregnant which is 6.7% &Anti TPO appeared more prevalent in euthyroid state in the 2nd trimester with prevalence 6.7% but appeared more with hypothyroidism in 3rd trimester 13.3% (Table III)

**Table (I):** Comparison between the ladies groups according to TSH (uIU/ml).

| | 3rd thermistor (n=30) | | 2nd trimester (n=30) | | 1st trimester (n=30) | | Non Pregnant (n=30) | | Test of Sig. | p |
|---|---|---|---|---|---|---|---|---|---|---|
| | No. | % | No. | % | No. | % | No. | % | | |
| **TSH (uiu/ml)** | | | | | | | | | | |
| Normal (0.27 – 4.2) | 23 | 76.7 | 24 | 80.0 | 24 | 80.0 | 24 | 80.0 | | |
| Abnormal low | 0 | 0.0 | 0 | 0.0 | 2 | 6.7 | 3 | 10.0 | $\chi^2$= 7.432 | 0.329 |
| Abnormal high | 7 | 23.3 | 6 | 20.0 | 4 | 13.3 | 3 | 10.0 | | |
| Min. – Max. | 0.75 – 6.77 | | 0.59 – 38.30 | | 0.01 – 7.10 | | 0.0 – 7.19 | | | |
| Mean ± SD. | 2.90 ± 1.73 | | 4.08 ± 6.66 | | 2.51 ± 1.78 | | 1.75 ± 1.66 | | $^{KW}\chi^2$=14.584* | 0.002* |
| Median | 2.56 | | 2.76 | | 2.14 | | 1.13 | | | |
| **Sig. bet. Grps** | $p_1$= 0.745, $p_2$=0.363, $p_3$=0.001*, $p_4$=0.211, $p_5$=0.002*, $p_6$=0.026* | | | | | | | | | |

$\chi^2$: Chi square test KW$\chi$2: Chi square value for Kruskal Wallis test

$p_1$: p value for Mann Whitney test for comparing between 3rd trimester and 2nd trimester

$p_2$: p value for Mann Whitney test for comparing between 3rd trimester and 1st trimester

$p_3$: p value for Mann Whitney test for comparing between 3rd trimester and Non Pregnant

$p_4$: p value for Mann Whitney test for comparing between 2nd trimester and 1st trimester

$p_5$: p value for Mann Whitney test for comparing between 2nd trimester and Non Pregnant

$p_6$: p value for Mann Whitney test for comparing between 1st trimester and Non Pregnant

*: Statistically significant at $p \leq 0.05$

**Table II:** Comparison between the studied groups according to FT4 (ng/dl).

| | 3rd trimester (n=30) | | 2nd trimester (n=30) | | 1st trimester (n=30) | | Non Pregnant (n=30) | | Test of Sig. | p |
|---|---|---|---|---|---|---|---|---|---|---|
| | No. | % | No. | % | No. | % | No. | % | | |
| **FT4 (ng/dl)** | | | | | | | | | | |
| Normal (0.9 – 1.8) | 14 | 46.7 | 23 | 76.7 | 25 | 83.3 | 26 | 86.7 | | |
| Abnormal low | 16 | 53.3 | 3 | 10.0 | 4 | 13.3 | 0 | 0.0 | $\chi^2$= 31.509* | <0.001* |
| Abnormal high | 0 | 0.0 | 3 | 10.3 | 1 | 3.3 | 4 | 13.3 | | |
| **Sig. bet. Grps** | $p_1$=0.001* , $p_2$ = 0.003*, $p_3$ <0.001* , $p_4$ = 0.703, $p_5$ = 0.273 , $p_6$ = 0.085 | | | | | | | | | |
| Min. – Max. | 0.58 – 1.70 | | 0.10 – 3.36 | | 0.35 – 2.50 | | 0.92 – 5.20 | | | |
| Mean ± SD. | 0.92 ± 0.24 | | 1.21 ± 0.56 | | 1.29 ± 0.48 | | 1.40 ± 0.78 | | KW$\chi^2$=25.892* | <0.001* |
| Median | 0.83 | | 1.10 | | 1.23 | | 1.20 | | | |
| **Sig. bet. Grps** | $p_1$= 0.001*, $p_2$<0.001*, $p_3$<0.001*, $p_4$=0.166, $p_5$=0.084, $p_6$=0.807 | | | | | | | | | |

**Table (III):** The difference between thyroid functions in the four groups.

| | 3rd trimester (n=30) | | 2nd trimester (n=30) | | 1st trimester (n=30) | | Total in pregnancy | | Non Pregnant (n=30) | |
|---|---|---|---|---|---|---|---|---|---|---|
| | No. | % | No. | % | No. | % | No. | % | No. | % |
| **Thyroid function** | | | | | | | | | | |
| Normal | 14 | 46.7 | 21 | 70.0 | 23 | 76.7 | 58 | 64.4 | 22 | 73.3 |
| Normal with anti TPO | 1 | 3.3 | 2 | 6.7 | 1 | 3.3 | 4 | 4.4 | 1 | 3.3 |
| Hypothyroidism | 6 | 20.0 | 1 | 3.3 | 0 | 0.0 | 7 | 7.7 | 0 | 0.0 |
| Hyperthyroidism | 3 | 10.0 | 1 | 3.3 | 1 | 3.3 | 5 | 5.5 | 2 | 6.7 |
| Hypothyroidism with +ve anti TPO | 4 | 13.3 | 3 | 10 | 0 | 0.0 | 7 | 7.7 | 0 | 0.0 |
| SUBCLINICAL Hypothyroidism | 2 | 6.7 | 1 | 3.3 | 3 | 10.0 | 6 | 6.6 | 2 | 6.7 |
| Subclinical hypo with anti TPO | 0 | 0.0 | 1 | 3.3 | 2 | 6.7 | 3 | 3.3 | 1 | 3.3 |
| Subclinical hyperthyroidism | 0 | 0.0 | 0 | 0.0 | 0 | 0.0 | 0 | 0 | 2 | 6.7 |

## Discussion:

Specific reference intervals for FT4, T4, and T3 in addition to TSH during pregnancy may be particularly important for several reasons. First, it would be important to know why the FT4 levels are in the first trimester and 2nd trimester higher than in the 3rd trimester in a euthyroid pregnancy, and this is the time when the fetus is wholly dependent on T4 from the mother. Accurate reference intervals for FT4 and FT3 would then provide the ability to detect a deficiency at this critical time and provide a subtle indication of maternal hypothyroidism. In our study there was significant difference between pregnant group and non-pregnant group in mean TSH, some cases may be subclinical or mild with normal FT4. In the pregnant ladies group; 28 ladies with abnormal thyroid function (31%): hyperthyroidism in 5 ladies (5.5%), hypothyroidism in 23 ladies (25.5%) and 19 ladies with anti -TPO +VE (21%).On the other hand, the present results were not concordant with some other studies in this field, in the Tunisian study done by Feki and his colleges;

the incidence of thyroid disorder in Tunisian determined TSH and TPO-Abs in 1519 pregnant ladies aged 17 to 47 years. Thyroid disorder was defined as hyperthyroidism (TSH≤0.10) or hypothyroidism (TSH >4.5 mIU/L), and/or positive TPO Abs (>12 IU/L). Thyroid disorders were observed in 147 pregnant ladies (9.7%). Positive TPO-Abs was noted in 99 ladies (6.5%), hypothyroidism in 48 ladies (3.2%) and hyperthyroidism in 10 women (1.3%).[7] In our study 1st trimester showed: prevalence of hypothyroidism 16.7% (5of 30) but all are subclinical cases due the stimulatory effect of HCG Compared to other study in USA reported by Cleary-Goldman where a total of 10,990 first- and second-trim ester serum assayed for TSH, FT4), and ant thyroglobulin and ant thyroid peroxidase antibodies. Subclinical hypothyroidism was documented in 2.2% (240 of 10,990) in the first trimester. Overt hypothyroidism was documented in 2.1% (232 of 10,990).[8] The wide gap observed in our study than other Tunisian and USA one is due to iodine deficiency that proved with increase demand for iodine with the advance in pregnancy. Hypothyroidism in our study is more in 3rd trimester may be due to lack of program that ensures proper nutrition for pregnant women and misuse of Pesticides by farmers, this leads to contamination of vegetables and fruits, which ultimately affects human health.

This gap reflects the magnitude of the problem that we discuss that major maternal and fetal complications will occur. So ministry of health should do proper situation analysis regarding diet and life style of pregnant women for detection of major causes for iodine deficiency and find cost effective plan to solve this major problem through collaboration of efforts of health and agriculture ministries and whole population to prevent further fetal and maternal complications. The prevalence of hyperthyroidism in pregnant women was 5.5% .more prevalent in 3rd trimester 10% of women compared with Tunisian study done by Feki and his colleges (1.3%), and (1%) in Gaza study. [7] also this study showed significant difference between TSH parameter in pregnant and non-pregnant women, mean TSH was higher in pregnant than non-pregnant it was initially increased in 1st trimester, increased more in 2nd trimester then decreased again in 3rd trimester. FT4 in the studied group showed significant difference between pregnant and non pregnant group, mean FT4 was lower in pregnant than non pregnant women and also it showed more decline with advance in pregnancy.

However FT3 parameter there was no significance between pregnant women and non- pregnant women, but it showed decline from 1st to 3rd trimester in mean of FT3. also there was no significant difference between pregnant and non-pregnant regarding anti TPO however it appeared more significantly in 3nd trimester (n=10) that maybe associated with hypothyroid hashimoto thyroiditis. Compared to other studies that measured the same parameters a Study in Tabriz-Iran (2005) (by Zarghami) was carried out to find out alterations in thyroid function tests in each trimester in normal pregnant women as compared to non-pregnant women. A case-control study designed with 229 normal pregnant and randomly selected non-pregnant healthy female controls. Mean age groups was 16-40 years. Thyroid function tests were carried out by measuring serum level s of TSH, FT4, and FT3. They found that mean FT4 was strongly decreased during the third trimester. Free T3 showed declining in the second and third trimesters that was similar to our study. But TSH did not show significant difference in each trimester compared with non-pregnant women that was different from our study. [9] On the other hand, the present results were not concordant with some other studies in this field. In India a case-control study designed by Pasupathi with two groups of women: 75 normal pregnant ladies randomly selected from the first trimester and randomly selected non-pregnant healthy ladies control that thyroid function tests were carried out by measuring the serum level s of (TSH), (FT4), and (FT3). The mean FT4 levels in the first trimester were non-significantly lower than that of the non-pregnant subjects. The pregnant groups' mean FT3 non-significantly higher than that of the non-pregnant ladies. The mean TSH levels of pregnant women were lower than the mean level of

non pregnant but was not significant, the same as we found in our study.[10] Also Kurioka and his colleagues reported significantly reduced levels of free T3 and free T4,[11] Kumar reported that TSH values were increased steadily with each trimester.[12] Anti TPO measured in three trimesters showed significant increasing with advance in pregnancy and cause hypothyroidism (hashimoto thyroiditis) and may be prolonged to postpartum thyroiditis.

## Conclusion:

From the results of this study we can conclude the followings: In our study 21.6% of the studied ladies were having hypothyroidism; 88.42 % of them were pregnant, 7.5% of the studied ladies were having hyperthyroidism; 55.5 % of them were pregnant. No correlation between age & thyroid parameter, significant difference between pregnant women and non pregnant regarding TSH & FT4 and no significant difference between pregnant and non pregnant regarding FT3 but the mean FT3 showed decline in pregnancy. There was discrepancy between FT4 &TSH in pregnancy due to presence of other stimulatory and inhibitory factors in pregnancy, however the increase in anti TPO titer in pregnancy was not significant in relation to non-pregnant; it showed significant increase during 3rd trimester.

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