Research Article

Assessment of Thyroid functions in a sample of Pregnant Women in El-Minia University Hospital

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Abstract

Background: About ٢ to ٥٪ of pregnant women suffer from any variety of thyroid disorders and timely intervention can be done if detected early.(١) Pregnancy may affect the course of thyroid disorders and, conversely, thyroid diseases may affect the course of pregnancy.(٢) During gestation, a significant amount of TPO-Ab- and/or TGAb- positive women are at risk of developing hypothyroidism, since they have lower thyroid function reserve.(٣) **Aim of the study**: The aim of this study is to detect the presence of thyroid function abnormalities and thyroid autoantibodies in a sample of pregnant women to detect If there is a relation between the presence of these thyroid autoantibodies and the abnormalities of thyroid functions. **Subject and Methods**: The study assesses the level of thyroid hormones and thyroid autoantibodies in ٨٨ pregnant women up to ١٣ week of gestation. **Results:** The present study revealed an abnormality in TSH level as it decreased in ٤ pregnant women (٤.٥٪) and raised in ٥ women (٥.٧٪). Thyroid autoantibodies were positive in ٢٤ pregnant women (٢٧.٣٪) as the anti TG antibody was positive in ٦ pregnant women (٦.٨٪) and the anti TPO was positive in ١٨ pregnant women (٢٠.٥٪). **Conclusion:** Normal thyroid function during pregnancy is essential to ensure delivery of a healthy baby, which may be achieved with frequent monitoring of thyroid function during gestation and cautious adjustment of medications during treatment.

Key words: pregnancy, thyroid functions, thyroid autoantibodies.

Introduction

Thyroid hormone plays a role in brain development during the fetal period, as different parts of the brain are differentially sensitive to thyroid hormone at any one time during development, and the sensitivity to thyroid hormone is controlled, in part, by local control of hormone production(٤). The thyroid abnormalities during the first trimester of pregnancy should be under specific and particular pregnancy medical care, due to fetus physiological demand particularly physical, mental and brain developments. Therefore, evaluation of thyroid function tests during pregnancy is of great importance to prevent the above abnormalities(٥)

The most frequent thyroid disorder in pregnancy is maternal hypothyroidism. It is associated with fetal loss, placental abruptions, pre-eclampsia, preterm delivery and reduced intellectual function in the offspring.(٦)

Positive thyroid peroxidase Antibody (TPO-Ab) and/or antithyroglobulin antibody (TG-Ab) test results are found in approximately ٥٪ of euthyroid pregnant women. However, a thyroid autoantibody prevalence of up to ١٥٪ has been found in pregnant populations.(٧) At parturition, ٥٦٪ of thyroid antibody-positive mothers have been reported to have high TSH values. During gestation, a significant amount of TPO-Ab- and/or TGAb- positive women are at risk of developing hypothyroidism, since they have lower thyroid function reserve(٣).

Chronic autoimmune thyroiditis is the most important cause of hypothyroidism in pregnant women, and up to ٩٠٪ of women with hypothyroidism during pregnancy are positive for thyroid antibodies.(٨)

Because many women remain asymptomatic, particular attention is required from the obstetrical care providers for this condition to be diagnosed and to evaluate more systematically thyroid function when women attend the prenatal clinic for the first time. Only thyroid function tests confirm the diagnosis.[٩]

Subjects and methods

This cross sectional study was conducted at in the outpatient clinics of Gynecology Obstetric Hospital El-Minia University in the period from November ٢٠١١to November ٢٠١٢, eighty eight pregnant women up to gestational age of ١٣ weeks selected randomly during the study period. Pregnant women were excluded if they already had thyroid disorders, receiving medical treatment for thyroid disorders, morbid obesity, history of ovarian hormonal therapy and women with Chronic medical disease (renal, hepatic, cardiac and autoimmune). Critically ill women were also excluded. All pregnant women were subjected to the following: Full history taking with respect to maternal age (over or under ٣٠ years as women over ٣٠ years are at increased risk to develop thyroid disorder during pregnancy [١٠], parity status (primigravida,multipara and grand multipara >٥ pregnancy)[١١] and if there was history of Abortion and menstrual history. Thyroid symptoms were also asked for as defined by Paul et al., ٢٠١٣[١٢] All participants were subjected to the following investigations. Hemoglobin level, fasting blood glucose, serum creatinine, thyroid function test (free T٣, free T٤, TSH). Measurement of thyroperoxidase antibodies (ATPO) and antithyroglobulin antibodies (ATG) levels by enzyme linked immunosorbent assay [ELISA].

Laboratory studies

Blood Sampling and Processing: ٥ml venous blood were drawn for routine laboratory assessments: Two ml of venous blood on EDTA containing tube for fasting blood glucose , heamoglobin level , serum creatinine determined by spectrophotometer. ٣ ml of the Collect blood specimens centrifuged and separate the serum immediately. Specimens had stored frozen at (-٢٠" C). Prior to assay, frozen sera was completely thawed and mixed well.

Principle of TSH assesement:

The assay system utilize a unique monoclonal antibody directed against a distinct antigenic determinant on the intact TSH molecule. Mouse monoclonal anti-TSH antibody is used for solid phase (microtiter wells) immobilization and a gout anti-TSH antibody is in the antibody-enzyme (horseradish peroxidase) conjugate solution. The normal range in the first trimister ٠.٠٥-٢.٥uIU/ml.[١٠]

Free Tri iodothyronine (T٣) level: using ELISA kits supplied from (The Diagnostic Automation Inc. company) in which cut off value equal to ١.٤ - ٤.٢ pg/ml.

Free Thyroxine (T٤) level: using ELISA kits supplied from (Chemux Bio Science, Inc. Company, USA) in which cut off value equal to ٠.٦٥–١.٩٧ ng/dL.

ANTI-TGA Titer Assay

Principle of the Test: Diluted patient serum is added to wells coated with purified TG recombinant antigen. TG specific antibody, if present, binds to the antigen. The intensity of the color generated is proportional to the amount of TG specific antibody in the sample. The normal range of ATGA index <١.٢ equal to<٧٥ IU/ml[١١].

ANTI-TPO Titer Assay

Principle of the test: Diluted patient serum is added to wells coated with purified TPO recombinant antigen. TPO lgG specific antibody, if present, binds to the antigen. the enzyme. The intensity of the color generated is proportional to the amount of lgG specific antibody in the sample. The normal range of A nti TPO index <١.٢ equal to<٧٥ IU/ml.[١٢]

Statistical Analysis

Data entry and analysis were done using software SPSS version ١٩, and microstats program. Graphics were done using Excel. Quantitative data were presented by mean and standard deviation, while qualitative data were presented by frequency distribution. Student t-test, and Z test used. The probability of less than ٠.٠٥ was used as a cut off point for all significant tests.

Results

The present study was conducted at Minia University in the out-patient clinics of Gynecology Obstetric Hospital, ٨٨ pregnant women up to gestational age of ١٣ weeks selected randomly during the study period from

November ٢٠١١ to November ٢٠١٢. The baseline characteristics of the ٨٨ enrolled pregnant women were as follow. Their mean age was ٢٦.٧ yrs ± ٦.٤. ٢٣.٩٪ (٢١ pregnant women) were primigravida, ٥٩٪ (٥٢ pregnant women) were multipara and ١٥٪ (١٧ pregnant women) were grand multipara (more than ٥ pregnancies). ٢١.٦ %[١٩] had history of previous abortion. Their gestational age was ٧-١٣ weeks with mean (١٠.٠٣±١.٩٥)

TSH level was raised in ٥ women (٥.٧٪) and decreased in ٤ pregnant women (٤.٥٪). Thyroid autoantibodies were positive in ٢٤ pregnant women (٢٧.٣٪). As the anti TG antibody was positive in ٦ pregnant women (٦.٨٪) and the anti TPO was positive in ١٨ pregnant women (٢٠.٥٪) **table** ١.

Table ٢ shows the correlation between clinical data and laboratory results of the studied group. TSH, TG Ab and the TPO Ab was negatively correlated with gestational age. In addition TPO Ab was negatively correlated BMI whereas the TG Ab was negatively correlated with the maternal age. The other laboratory data showed insignificant correlation results.

TSH abnormalities were mainly in multiparous women as it raised in ٧.٧٪ (٤ multiparous) and decreased in ٥.٨٪ (٣ multiparous). TPO ab was elevated in ٢١.٢٪[١١] multi-para and TGA ab was elevated in ٥.٦٪[٥] multiparous. However these changes did not achieve statistically significant results.

The TPO ab positivity had no relation to the abnormalities in the TSH level as the TPO was positive in ٢٠.٥٪ (١٨ pregnant women) ٢ of them had raised TSH and the others had normal TSH . The same was observed for the TGA ab and TSH level.

There was a significant relation between the TG ab and the T٤ level as the p value was ٠.٠٣ as shown in table ٣.

Tables (٤); revealed the correlation studies between the laboratory parameters and clinical variables. Plasma TSH showed significant correlation with anti-TPO antibodies (P=٠.٠٢٥). Plasma T٣ showed highly significant correlation with plasma T٤ (P=٠.٠٠٠).TSH level in regressive analysis was related significantly with the anti TPO as shown in table ٤.

Table (١): distribution of thyroid function and thyroid antibody according to normal values

Thyroid functions		Frequency (NO=٨٨)	Percent
TSH	**normal**	٧٩	٨٩.٨
	Raised	٥	٥.٧
	decreased	٤	٤.٥
T٤	**normal**	٧٨	٨٨.٦
	raised	٨	٩.١
	decreased	٢	٢.٣
T٣	**normal**	٨١	٩٢.٠
	Raised	٧	٨.٠
	decreased	٠	.٠
Anti TGA titer	**Raised**	٦	٦.٨
	normal	٨٢	٩٣.٢
Anti TPO titre	**Raised**	١٨	٢٠.٥
	normal	٧٠	٧٩.٥

TSH= thyroid stimulating hormone, T٣=tri-iodothyronine, T٤=thyroxin Anti TGA=anti- thyroglobuin antibodies,Anti- TPO =Thyro-peroxidase antibodies

Table (٢): Correlation between age and thyroid hormones in studied group

Variables		Maternal age	Gestational age	BMI
TSH	r	٠.١٩	٠.٠١٢-	٠.٠٦
	p	٠.٠٧	٠.٩	٠.٥
T٣	r	- ٠.٢٣	٠.٢٤	-٠.٠١٢
	p	٠.٠٢*	٠.٠٢	٠.٢
T٤	r	- ٠.٠٧	٠.١٨١	٠.٠٢٢
	p	٠.٤	٠.٠٩	٠.٨
TPO-Ab	r	٠.٠٠٨	-٠.٠٢	-٠.٠٧
	p	٠.٩	٠.٨	٠.٥
TGA Ab	r	-٠.٠٦٦	-٠.٠٣١	٠.٠١٥
	p	٠.٥	٠.٧	٠.٨

Table (٣): Relation between T٤ and TG ab

T٤		TGA ab		Total	p
		raised	normal		
	Normal	٤	٧٤	٧٨	٠.٠٣
		٦٦.٧٪	٩٠.٢٪	٨٨.٦٪	
	Decreased	١	١	٢	
		١٦.٧٪	١.٢٪	٢.٣٪	
	Raised	١	٧	٨	
		١٦.٧٪	٨.٥٪	٩.١٪	
Total		٦	٨٢	٨٨	
		١٠٠.٠٪	١٠٠.٠٪	١٠٠.٠٪	

Table (٤): Correlation between thyroid hormones and thyroid antibodies

		TSH	T٤	T٣	TGA ab	TPO ab
TSH	Pearson Correlation		-.١٧٢	.٠٩٩	-.٠١٩	.٢٣٩*
	Sig. (٢-tailed)		.١٠٩	.٣٥٧	.٨٦٠	.٠٢٥
	N		٨٨	٨٨	٨٨	٨٨
T٤	Pearson Correlation	-.١٧٢		.٤٠٢**	.٠٧٥	.٠٧٢
	Sig. (٢-tailed)	.١٠٩		.٠٠٠	.٤٨٦	.٥٠٣
	N	٨٨		٨٨	٨٨	٨٨
T٣	Pearson Correlation	.٠٩٩	.٤٠٢**		.١٤٩	.١٦١
	Sig. (٢-tailed)	.٣٥٧	.٠٠٠		.١٦٧	.١٣٣
	N	٨٨	٨٨		٨٨	٨٨
TGA ab	Pearson Correlation	-.٠١٩	.٠٧٥	.١٤٩		.٠٨١
	Sig. (٢-tailed)	.٨٦٠	.٤٨٦	.١٦٧		.٤٥٥
	N	٨٨	٨٨	٨٨		٨٨
TPO ab	Pearson Correlation	.٢٣٩*	.٠٧٢	.١٦١	.٠٨١	
	Sig. (٢-tailed)	.٠٢٥	.٥٠٣	.١٣٣	.٤٥٥	
	N	٨٨	٨٨	٨٨	٨٨	

Table (٥): multiple regressive analyses for TSH

TSH	Standarizied coefficient Beta	T	Sig
Age	.٢٧٦	١.٤٩١	.١٤٠
Gestational age	.٠٠٥	.٠٤٥	.٩٦٤
Abortion	-٠.٥٨	-.٥١٥	.٦٠٨
Parity	.٠٤٨	.٣٠٣	.٧٦٣
BMI	-.٠٦٠	-.٤٦٢	.٦٤٥
Hb	-.٠٢٦	-.٢٣٠	.٨١٩
ATG-ab	-.٠٤٤	-.٣٩٢	.٦٩٦
ATPO-ab	.٢٥٣	٢.٢٧٨	.٠٢٥

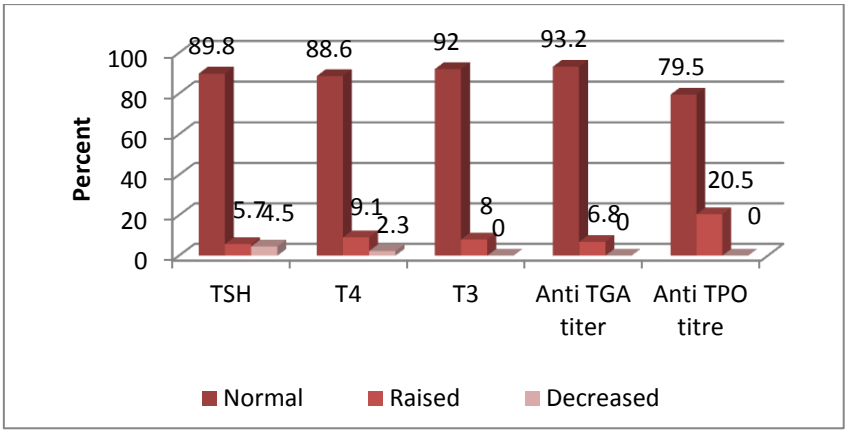

Figure (١): Distribution of thyroid functions & thyroid antibodies in the studied groups

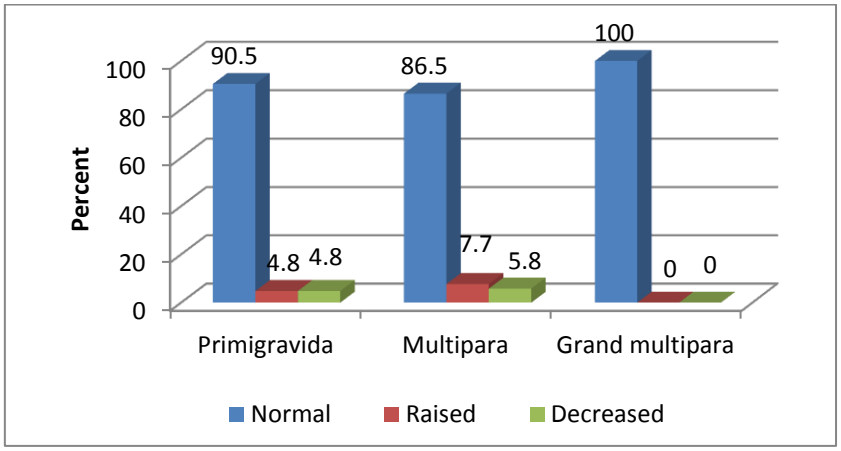

Fig.٢: Relation between TSH and parity

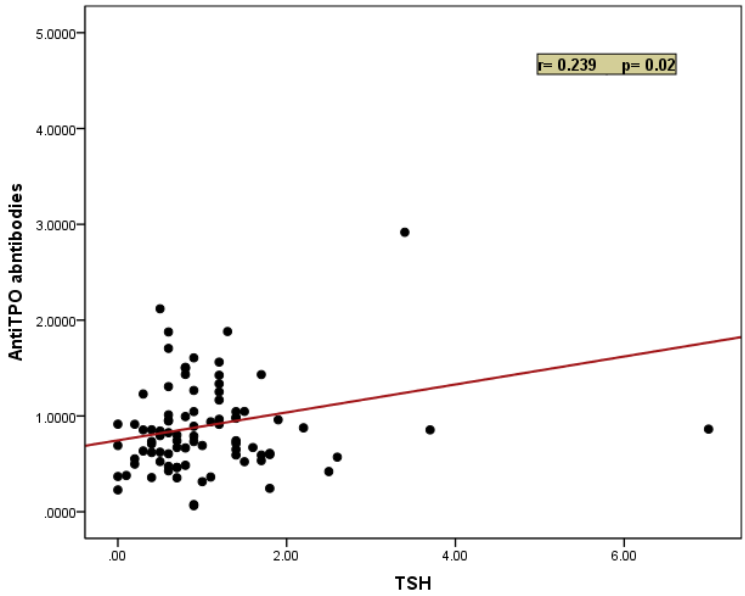

Fig. ٣: Correlation between TSH and anti-TPO antibodies

Discussion

There is a high incidence of thyroid dysfunction during pregnancy resulting in adverse maternal and fetal effects which may justify screening for thyroid function during early pregnancy[١٦]. Evaluation of thyroid status in pregnancy requires an understanding of pregnancy-associated changes in thyroid function tests and how they vary by trimester[١٧]. During pregnancy and after delivery, the maternal thyroid gland faces several metabolic, hemodynamic and immunologic changes. Thyroid autoimmunity ameliorates during pregnancy and aggravates after delivery[١٨,١٩]. The circulating levels of thyroid-binding globulin (TBG) are also increased by estrogen stimulation. On the other hand the increased renal clearance both fetal intake and placenta metabolism induce a relative decline in the availability of iodide[٢٠].

In the present study; ٥.٧٪ of subjects showed raised plasma TSH.

Measurement of serum TSH is the first-line screening variable for thyroid dysfunction in pregnancy[٢١]. Peripheral thyroid hormone values are highly different among laboratories, and there is a need for laboratory-specific gestational age-related reference ranges. The best laboratory assessment of thyroid function is a free thyroid hormone estimate combined with TSH[١٩,٢٠]

The prevalence of moderately elevated TSH levels consistent with subclinical hypothyroidism (٢.٥-٤.٠ IU/mL) was ٢٣٪ in a cohort of ١,٢٣١ women pursuing assisted reproductive technologies[٢٠]. There is a greater prevalence of subclinical hypothyroidism in women with delivery before ٣٢ weeks. Higher maternal TSH levels even within the normal reference range are associated with an increased risk of miscarriages, fetal and neonatal distress and preterm delivery[٢٢].

In the study of Dal-Lago et al., (٢٠١١) they found that the mean basal TSH serum levels were higher (P<٠.٠٠١) in repeated miscarriage women compared with the controls. A transient impairment of thyroid function in early pregnancy may be implicated in repeated abortions[٢٣].

The current study results differ from those of Stagnaro-Green et al., (٢٠١٢)

who found that TSH values decline during the transition from pre-pregnancy to early pregnancy. Serum TSH levels decrease in the first trimester and increase in the second and third trimesters; however, not to pre-pregnancy levels[٢٤].

In the current study; T٣ showed significant inverse correlation with gestational age and history of previous abortions

Younger age and being in gestational weeks ١-٨ were significant risk factors for hypo-

thyroidism. They suggested that the reference criteria need revision, and that pathology laboratories should adopt appropriate pregnancy-specific reference intervals[٢٥].

Several recent recommendations to use total thyroxine measurements in the diagnosis of thyroid function in pregnancy (in particular, "Clinical Practice Guidelines for Hypothyroidism in Adults," cosponsored by the American Thyroid Association and the American Association of Clinical Endocrinologists, which promote the use of Total over free Thyroid hormones[٢٦].

Accordingly FT assays that fully compensate for serum TBG concentrations should discriminate dysfunctionality from normality more efficiently than total hormone measurements, whether in pregnant or non-pregnant states. The difficulties in FT measurement arise from inconsistent calibration of present-day commercial assays. This finding questions the recommendation that total hormone assays should supersede the former in pregnancy[٢٧].

In the current study those women with raised titre of TPO antibodies were (٢٠.٥٪) and those with raised titre of TG antibodies were (٦.٨٪). T٤ showed significant correlation with TGA antibodies and insignificant one with anti-TPO antibodies. Meanwhile; T٣ showed insignificant correlation with both groups of antibodies. On the other hand TSH showed significant correlation with anti-TPO antibodies and insignificant one with anti-TGA antibodies. The current results agreed with those of Ashoor et al., (٢٠١٠) as they found ١٦.٨ % of pregnant women were positive for one or both anti-thyroid antibodies. This difference may be related to the difference in the numbers of both groups.[٢٨]

At least ٥-١٠٪ of women showed positive titre for thyroid antibodies and have an increased risk of developing a certain degree of thyroid insufficiency during pregnancy (Krassas et al., ٢٠١٠).[٢٩]

The results of the present result was much higher than that of Wang et al., (٢٠١١); who found that the TPO abs was positive in ٩.٦٪ of cases only[٣٠]. TPO-ab is suspected to be associated with an increased risk of fetal loss, premature delivery and hypothyroidism[٣١].

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