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Anti-Thyroid Peroxidase Antibodies Positivity throughout Pregnancy

Fatin N. KassabBashi[1], Hazim A.Mohammed[1], Rana M. Raoof[2]
[1] Department of Biochemistry,College of Medicine, University of Mosul, Mosul, Iraq.
[2] Department of Anatomy, College of Medicine, University of Mosul, Mosul, Iraq.

ABSTRACT

Thyroid disorders are among the most common endocrine disorders affecting pregnant women. Thyroid autoimmunity is among these disorders and anti-thyroid peroxidase antibodies is considered as the most common of thyroid antibodies .Different physiological changes take place throughout the progress of normal pregnancy and affect the thyroid functions, therefore thyroid function tests (thyroid stimulating hormone, free thyroid hormones FT3 and FT4) will differ in pregnant than non-pregnant woman as well will differ along the three trimesters of pregnancy.

Key words
Thyroid peroxidase antibodies, thyroid function tests,trimester of pregnancy.

Introduction

Normal pregnancy is usually associated with thyroid hormones(THs) changes including :increase in thyroxin binding protein (TBG) , increase in TH production ,and thyroid stimulatory effect of human chorionic gonadotropin (hCG)[1].All of these factors will influence the thyroid function tests (TFTs) during pregnancy, healthy thyroid gland will adapt to these alterations through changing the TH metabolism, iodine intake , and the hypothalamic- pituitary-thyroid axis[2].

Therefore healthy pregnant TFTs will differ from those of healthy non pregnant women[1].Following conception, both circulatory TBG and total thyroxin TT4 concentrations will increase by the 7thweekof gestation, reaching the peak by approximately week 16 of gestation, and then remain high until delivery[3].

In the first trimester of pregnancy, maternal hCG will directly stimulate the thyroid stimulating hormone TSH receptor, increasing the TH production, resulting in subsequent reduction in serum TSH concentration [4].

Therefore during pregnancy women will have lower serum TSH concentration than prior to pregnancy [1].Serum TSH and its reference range will gradually rise during the second and third trimester of pregnancy but remain lower than in non-pregnant women[5].

In women with multiple pregnancies , serum hCG concentrations tend to be higher , while TSH concentrations tend to be lower, for this reason, the downward shift in TSH reference interval is greater in multiple pregnancies than singleton ones[6].

Regarding THs synthesis both thyroglobulin Tg and thyroid peroxidase TPO enzymes play a vital role in THs synthesis and secretion, TSH stimulates the expression of Tg through the TSH receptor , but this expression is not TSH dependent ,as it can be maintained by insulin like growth factor IGF-1 and other growth factors[7].

Thyroid peroxidase was discovered primarily as thyroid microsomal autoantigen by Belyavin and Trotter in 1959 [8], it took 20 years later to be characterized as TPO by Portman and his colleagues [9].TPO enzyme is membrane bound , not secreted into the circulation ,not cause anti thyroid peroxidase antibodies ATPO to be removed or blocked from being measured[10].

The TPO gene which is located on chromosome 2p25 is also regulated by TSH, but is much more transcriptionally TSH dependent than Tg with its expression lost in the absence of TSH. It is approximately 107 KD expressed mostly on the apical surface of thyrocytes, catalyzing the coupling of two molecules of diiodotyrosin DIT or one molecule of DIT with monoiodotyrosin MIT forming tetraiodothyronine T4 and triiodothyronine T3, respectively which will then be stored in the colloid as part of Tg molecule [11].

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Aim of the study

To record the presence of ATPO positive women throughout pregnancy in Mosul city, Iraq.

Material and Method

One hundred eighty apparently healthy pregnant women with different gestational ages were recruited to this study which was performedat AL-Khansaateaching Hospital, and AL-Noor Primary Health Care Centre in Mosul, Iraq .From the period 1st Jan. to 1st Apr.2021. The excluded cases were those with past history of thyroid disorders, history of autoimmune disease, twin pregnancy, past medical history of any of the following (hypertension, diabetes mellitus, cardiac,hepatic, renal disorders) or the administration of any of the thyroid altering drugs.

After explaining the aimof the study and obtaining a consent from the participants, the following data was recorded: name, age, parity , gravid, abortion, mode of delivery of previous pregnancies, weight, height, gestational age calculated according to the last menstrual cycle or early ultrasound, according to which participants were classified into three groups:FIRST trimester, SECOND trimester and THIRD trimester groups.

There were sixty participant per each group ,with the exclusion of 3 , 5 , and 6 participants from the 1st , 2nd , and 3rd group respectively because they met at least one of the exclusion criteria.

Each participant was interviewed alone and submitted to general examination and exclusion of goiter , then 3-5 ml of venous blood was drawn , let to agglutinate ,then centrifuged at (2000 rpm)for 10 minutes to obtain serum to be examined for TFTs including TSH , and free thyroid hormones (FT3 and FT4), as well as Anti-Thyroid Peroxidase Antibodies ATPO.

TFTs were performed by an electrochemiluminscence technique using Access 2 Beckman coulter NHANES,USA with TSH reference interval ranging between(0.24-5.4 µ IU/mL) ,FT3 (2.5-3.9 pg/ml), and FT4(0.6-1.6 ng/dl).While ATPO level was measured using ELISA technique by ORGENTEC Diagnostika GmbH, Germany, possessing a measuring range (0-3000 IU/ml)and cutoff value of 75 IU/ml accordingly any reading >75 considered as positive ATPO

Statistical analysis was done using ANOVAtest, SPSS version 26.

Results

Our study shows that ATPO positive cases in the 1st trimester were 7/57(12.28%), 2nd trimester 5/55(9.09%), while in 3rd trimester (7.40%) respectively.

Regarding TFTs,the following tablessummarize their findings.

Table (1):FT3 variations in the ATPO positive cases among the three trimesters

FT3	No.	Rangepg/ml	Mean±SDpg/ml	95% CI of meanpg/ml
1st trimester	7/57	2.82-3.80	3.24±0.36	2.90-3.57
2nd trimester	5/55	2.30-2.64	2.50±0.14	2.32-2.68
3rd trimester	4/54	2.00-2.60	2.35±0.25	1.95-2.76

*p-value by anova test was <0.0001.

Table (2):FT4 variations in the ATPO positive cases among the three trimesters

FT4	No.	Rangeng/dl	Mean±SDng/dl	95% CI of meanng/dl
1st trimester	7/57	0.68-2.00	1.06±0.44	0.65-1.47
2nd trimester	5/55	0.47-1.13	0.82±0.26	0.49-1.14
3rd trimester	4/54	0.56-1.03	0.80±0.19	0.49-1.11

*P- value by anova test was 0.3

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Table (3):TSH variations in the ATPO positive cases among the three trimesters

TSH	No.	RangeμIU/mL	Mean±SDμIU/mL	95% CI of meanμIU/mL
1st trimester	7/57	1.19-4.05	2.08±1.05	1.10-3.05
2nd trimester	5/55	0.90-5.38	2.2-±1.83	-0.01-4.52
3rd trimester	4/54	0.78-5.38	2.47±2.02	-0.75-5.70

*P- value by anova test was 0.9

Table (4): ATPO variations in the ATPO positive cases among the three trimesters.

ATPO	No.	Range IU/ml	Mean±SD IU/ml	95% CI of mean IU/ml
1st trimester	7/57	165.80-2250.00	965.15±806.88	218.91-1711.39
2nd trimester	5/55	77.50-975.00	292.70±384.24	-184.40-769.80
3rd trimester	4/54	88.30-152.00	108.47±30.04	60.66-156.28

*P- value by anova test was 0.06

Discussion

Our study showed lower TSH concentration during the first trimester of pregnancy in ATPO positive women followed by subsequent elevation as pregnancy progress (second and third trimester). A similar finding reported by Glinoer et al[2]who noticed 10% reduction in the fraction of women with suppressed TSH during the 2nd trimester versus 5% reduction in the 3rd trimester,simultaneously , Alexander et al[1] found that in ATPO positive women the TSH concentration will increases as pregnancy progress from a mean of 1.7 m IU/L at (12)week to 3.5 m IU/L at term.

Glinoer et al[2]also noticed that ATPO titer were highest in the 1st trimester of pregnancy and their titers decrease as pregnancy proceed ,this finding was also reported 12 years later when Negro et al[12] in a prospective study noticed a reduction in ATPO antibodies over the progress of gestation as well as Balucan F S et al[10]who also stated a decrease in ATPO level throughout pregnancy reaching a nadir in the third trimester with their rebound appearance causing postpartum thyroid disease. In addition Tingi E et al[13] concluded that autoimmune thyroid disorders tend to improve throughout pregnancy ,but commonly flare up in the postpartum period .

These findings coincide with our results of the highest ATPO level at first trimester followed by subsequent reduced incidence and concentrations.

The interpretationof both FT3 and FT4 is difficult during pregnancy because of higher TBG and LOWER albumin that decrease the accuracy of immunoassays causing falsely low levels, however a general consensus of transient rise in FT4 during the first trimester due to relatively high circulating h CG followed by FT4 reduction in second and third trimester albeit with normal reference range[14].

Very little data was available regarding FT3and FT4 changes in ATPO positive cases although our study noticed their reduction with the progress of pregnancy.

Conclusion

The percent of ATPO positivity in different trimesters of pregnancy was similar elsewhere and it was highest in the 1st trimester than others.

Recommendation

Since our locality is a well-known for iodine deficiency so ATPO is recommended as screening test n: during pregnancy.

Conflicts of interest

There are no conflicts to declare.

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