Assessment of the relation of anti-TPO and TSH, T3 and T4 levels between some subclinical diabetes patients in Iran

ABSTRACT

As we know, around 28% of ills who had benign fibrocystic mastopathy mostly have shown antibodies of anti-TPO as well as around 80% of them that have shown the thyroid hypertrophy issue. The Assessment of thyroid peroxidase (TPO) as the main antigen agent of the thyroid microsomal fraction has enabled the progress of a sensitive and specific assay for the detection of the corresponding autoantibodies and other digestive fractions. Effect of gender, climate, and age on the ATPO, TSH, T3 and T4 rates was assessed as a goal. We evaluated the diagnostic validity of the anti-TPO, TSH, T3, and T4 assays and their relationships in 500 laboratory cases from Isfahan province with various types of thyroid and diabetes diseases and in controls. Age factor in the various levels of T3, T4, ATPO and TSH items is studied in the following research, which demonstrates a reduced rate in T4 factor of the 1st decade. In the present study, we concluded that patients with high TSH levels had high TPO tests. Patients with high levels of ATPO usually had high TSH, and in patients with low thyroid status, high TSH and high ATPO, TSH levels were normalized with levothyroxine tablets. Those with a high ATP content and normal TSH levels may have hypothyroidism in the future. You should check the thyroid test every 6 months. This could be concluded from the following research that gender, age, race, and area all demonstrate some remarkable impacts on the levels of T4, T3, TSH, and ATPO.

Keywords: Anti-TPO, TSH, T3, T4, Isfahan

Introduction

We recognized thyroid hormones such a remarked regulator and modulator of the biochemical pathways. Dysfunction of thyroid is famed in medical sciences and has highlighted terms. AITD (Autoimmune thyroid disease) is known as the most important reason of Hypothyroidism issue and is featured by the anti-thyroid antibodies presentation. AITD is famed as usual organ-specific autoimmune issue which mostly observed in females between 30to50. This disorder appears cause of lack of tolerability to TPO (autoantigens thyroid peroxidase), TG (thyroglobulin) and, TSH-R (thyroid stimulating hormone receptor [1]. It can be said about TPO (Thyreoperoxidase) as an enzyme which plays a role in membrane that shows a main part in synthesis system of thyroid hormone. Finally, T3 and T4 production were made by tyrosine successive and iodination coupling which was catalyzed by TPO .we know, the onset of autoimmune thyroid disease (ATD) could be started by inadequate immunological response against TPO triggers. Anti-TPO, as an antibody-mediated cytotoxicity inducer also plays a role for complementing the cascade activation and it might be responsible for directly inhabitant of TPO activity. As a result, both thyroid cell damage and direct enzyme blocking, might cause to inadequate hormone production, which can be seen by transient hyperthyroidism. It also clear that both hypo- and hyperthyroidism are known as the highlighted endocrine issues [2]. Around 1% of men and 2–4% of women have shown affectivity by AITD (autoimmune thyroid disease). Iodine supplementation has confirmed to be applicable in hypothyroidism, but continuous iodine exposure probably lead to hypo or hyper thyroidism, goiter and thyroid autoimmunity. Two highlighted consequences of AITD include Hashimoto's thyroiditis and Graves disorders. Other examples affected by AITD include atrophic autoimmune hypothyroidism, postpartum thyroiditis, and thyroid-associated orbitopathy [3]. Although AITD occurs in only 1% of the population, subclinical and focal thyroiditis and circulating anti-thyroid antibodies may be

found in 15% of euthyroid subjects [4]. Increasingly, elevated titers of ATPO were achieved by high range of disorders affecting different body organs, including viral hepatitis treated with INFα, breast cancer, Biermer's, pernicious anemia, insulin-dependent diabetes mellitus, thyroid nodular disorder, systemic lupus erythematosus and vitiligo. Moreover, some well-known items are distinguished by the relationships between obstetric issues and ATPO like depression after work [5]. Moreover thyroid dysfunction is associated with morbidity and deleterious outcomes such as increased risk of coronary artery disease and cardiovascular mortality [6]. In spite of the following data, confusion partly would be made by the detection of TPO antibodies: It must say that distinguishing detector of immune-assay issues applies as a feature for the characteristics of AITD, and ATPO might be explored in 10 percentage of the groups without overt thyroid failure. Increasingly, the effect of raised ATPO on the further dysfunction of thyroid is being questioned, too. Several investigations have demonstrated the relationship of ATPO in blood and risky thyroid impairment. As we seen, in some euthyroid patients that will never detect inadequate hormone production, TPO antibodies are increased [7]. Furthermore, the unknown section is the issue of the relationship between thyroid dysfunction and ATPO, and after primitive assessments, discovering the remarked level of ATPO that is diagnostic for any special thyroid disorder would open the new ways for this subject. This way was applied in the following research: increasing the antibodies of TPO might make a lot of differentiations in various types of thyroid disorders. So, in an Iranian groups of patients with variety of hormonal thyroid status, the presence of ATPO was investigated, and the relationship between thyroid role and ATPO were calculated.

Materials and methods

In this research, 500 laboratory cases (Random cases of 5 laboratories) from Isfahan city were included. Anti-TPO antibody was measured using enzyme-linked immunosorbent assay (ELISA) method (Radim Co, Italy). Then, by using enzyme-linked immunosorbent assay (ELISA) method (Radim Co, Italy), Serum TSH, T3, and T4 were measured. Determinations in the following ranges were considered normal:T3=0.9-3.2nmol/L, T4=50-170 nmol/L, TSH= 0.3-4 mlu/ml and ATPO< 75 U/mL Data regarding age and sex of participants were also recorded. Statistical analyses were performed using Chi-Square and Pearson correlation tests. P-values less than 0.05 were statistically significant.

Results

In the present study, the serum concentrations of ATPO, T4, T3, and TSH were measured in 500 individuals belonging to the area of Isfahan city (Center of Iran). The Mean for T4 in the female was 117.25 nmol/L and in the male was115.58 nmol/L with the range 50–170 nmol/L and for T3 it was found to be in the female 2.07nmol/L as the same as in the male 2.07 with a range of 0.9–3.2 nmol/L. The normal range for TSH was found to be 0.3–4 mlu/mL and the mean for TSH observed in the female was 3.32 U/mL and in the male was 3.27 U/mL. The mean for ATPO in the female was 430.78 U/mL.,which is higher than in the male 339.96 U/mL. Moreover, the normal value for ATPO was <75 U/mL. Purpose was watching the effect of age, gender, and climate on the ATPO, T4, T3, and TSH rates. The normal hormonal levels are various for variety of genders [8]. The age-wise distribution of research individuals for the detection of thyroid hormone (T3,T4 ,TSH) and ATPO levels is expressed in Tables [1,2,3, and 4]. The study subjects were divided into eight different age groups. It is almost clear from the data in table-1 that the serum value of T3 is significantly lower in females 1.50

nmol/L than in males 2.17 nmol/L in the age more than 80 years. The table-2 showed that serum T4 value increases significantly in the females 117.79 nmol/L than in males 111.21 nmol/L in the fifth decade of life, then, decreased significantly in the females 95.50 nmol/L than in males 122.20 nmol/L in age groups having more than 80 years. The illustrated data in table-3 showed that serum TSH value is significantly higher in females 3.63 mlu/ml than in males 2.68 mlu/mL in the second decade of life with a sudden drop in the fourth decade with high significant decrease in females 2.72 mlu/ml than in males 5.04 mlu/ml, then significantly returned to increase in the females 9.25 mlu/ml than in the males 1.37 mlu/ml in the over 80 years old age groups. While the provided data in table-4 revealed that there were a significant increases in serum ATPO values in females in the first and second decades of life (331.38 U/ml,454.55 U/ml) than in males (118.00 U/ml, 311.07 U/ml).The table also reveals that there was no significant differences observed in other age groups. The present work also examines the effect of age on T4,T3,TSH, and ATPO [Tables 7 and 8].

Table 1: Mean T3 levels by sex and age group. P-values refer to comparisons between men and women of the same age group.

Age	Mean		T test for mean difference		
	Female	Male	t statistic	p-value	Std. error
11-20	3.54	2.20	0.25ns	0.81	0.11
21-30	2.68	2.12	-1.05ns	0.30	0.07
31-40	2.62	2.12	-1.49ns	0.14	0.07
41-50	5.04	1.98	1.56ns	0.12	0.07
51-60	3.44	1.96	1.34ns	0.18	0.08
61-70	3.23	2.03	0.21ns	0.84	0.12
71-80	3.66	2.01	-0.59ns	0.56	0.19
≥80	1.37	2.17	-2.17*	0.05	0.32

* Significant at the 0.05 probability level; ns, not significant.

Table 2: Mean T4 levels by sex and age group. P-values refer to comparisons between men and women of the same age group.

Age	Mean		T test for mean difference		
	Female	Male	t statistic	p-value	Std. error
11-20	126.18	114.50	1.52ns	0.15	7.71
21-30	119.41	116.98	0.79ns	0.43	3.08
31-40	116.79	117.47	-0.23ns	0.82	2.98
41-50	114.44	116.07	-0.10ns	0.92	3.67
51-60	117.79	111.21	1.94*	0.05	3.57
61-70	117.68	111.20	0.94ns	0.35	6.92
71-80	111.38	118.50	-0.74ns	0.48	9.68
≥80	95.50	122.20	-3.50*	0.02	7.63

* Significant at the 0.05 probability level; ns, not significant.

Table 3: Mean TSH levels by sex and age group. P-values refer to comparisons between men and women of the same age group.

Age	Mean		T test for mean difference		
	Female	Male	t statistic	p-value	Std. error
11-20	3.23	3.54	-0.28ns	0.79	1.12
21-30	3.63	2.68	1.93*	0.05	0.55
31-40	3.12	2.62	1.13ns	0.26	0.44
41-50	2.72	5.04	-2.73**	0.01	0.83
51-60	3.56	3.44	0.14ns	0.89	0.86
61-70	3.70	3.23	0.34ns	0.74	1.41
71-80	4.83	3.66	0.51ns	0.62	2.29
≥80	9.25	1.37	2.92*	0.03	2.70

* Significant at the 0.05 probability level; ns, not significant.

Table 4: Mean ATPO levels by sex and age group. P-values refer to comparisons between men and women of the same age group.

Age	Mean		T test for mean difference		
	Female	Male	t statistic	p-value	Std. error
11-20	331.38	118.00	1.94*	0.05	110.28
21-30	454.55	311.07	1.96*	0.05	81.34
31-40	457.42	410.65	0.54ns	0.59	87.07
41-50	412.75	426.19	-0.13ns	0.90	94.19
51-60	412.78	266.85	1.38ns	0.17	105.51
61-70	354.58	274.93	0.58ns	0.56	137.04
71-80	754.88	250.50	1.63ns	0.13	309.97
≥80	1134.50	226.60	1.51ns	0.19	600.40

* Significant at the 0.05 probability level; ns, not significant.

Table 5: T4,T3,TSH, and ATPO in female levels by age group.

Age	ATPO	TSH	T3	T4
11-20	331.38	3.23	3.54	126.18
21-30	454.55	3.63	2.68	119.41
31-40	457.42	3.12	2.62	116.79
41-50	412.75	2.72	5.04	114.44
51-60	412.78	3.56	3.44	117.79
61-70	354.58	3.70	3.23	117.68
71-80	754.88	4.83	3.66	111.38
≥80	1134.50	9.25	1.37	95.50

Table 6: T4,T3,TSH, and ATPO in male levels by age group.

Age	ATPO	TSH	T3	T4
11-20	118.00	3.54	2.20	114.50
21-30	311.07	2.68	2.12	116.98
31-40	410.65	2.62	2.12	117.47
41-50	426.19	5.04	1.98	116.07
51-60	266.85	3.44	1.96	111.21
61-70	274.93	3.23	2.03	111.20
71-80	250.50	3.66	2.01	118.50
≥80	226.60	1.37	2.17	122.20

* Significant at the 0.05 probability level; ns, not significant.

Table 7: Comparison of T4,T3,TSH, and ATPO between the male and female age groups.

Genus	Statistics	Age	T4	T3	TSH	ATPO
Female	N	337	337	337	337	337
	Min	6	62	1.05	0.01	9.3
	Max	82	185	3.35	23	2200
	Mean	42.26	117.25	2.07	3.32	430.78
	Error of mean	0.79	0.99	0.02	0.18	25.42
Male	N	208	208	208	208	208
	Min	14	42	0.95	0.05	9.8
	Max	88	171	2.97	25.5	1980
	Mean	41.95	115.58	2.07	3.27	339.96
	Error of mean	1.06	1.20	0.02	0.24	32.58

Table 8 : T4,T3,TSH, and ATPO Levene's test for variance and T test for mean difference in various age groups

Parameters	Levene's test for equality of variances		T test for mean difference			Mean	
	F value	*p-value*	t statistic	*p-value*	Std. error	Female	Male
Age	0.22	0.639	0.236^{ns}	0.814	1.3	42.26	41.95
T4	1.897	0.169	1.062^{ns}	0.289	1.5	117.25	115.58
T3	0.553	0.457	-0.087^{ns}	0.931	0.03	2.07	2.07
TSH	0.001	0.976	0.166^{ns}	0.868	0.29	3.32	3.27
ATPO	0.092	0.762	2.201*	0.028	41.2	430.78	339.96

* Significant at the 0.05 probability level; ns, not significant.

Discussion

Iodine deficiency and related disorders were widespread in Iran prior to 1996, when universal salt iodization (USI) was implemented and in 2000 Iran was declared iodine deficiency disorder (IDD) free [9]. Now The national survey showed that salt intake among Iranian population is almost two times more than the level recommended by the WHO [10-13]. In some regions where lack of iodine deficiency is not seen, autoimmunity is considered as the whole reason of thyroid disorder, from hyperthyroidism to hypothyroidism. Raised rates of anti-Tg and anti-TPO antibodies are mostly related to thyroid autoimmune disorders and thyroid cancers, but low concentrations are also seen in normal subjects. Thyroid antibody is secreted in a Mendelian dominant method and it is found mostly in young females and relatives of autoimmune thyroid disease (AITD) patients. In this research, we discovered increased rates of anti-TPO in 17% women and 25% of men with normal TSH rates (Table 2) [14]. The level of T3 in men has shown rising, that was led by decreasing then it raised in the

further periods. Moreover, this model of impacts is coordinated with previous studies [15]. As we seen in women, it was mostly constant at first with a bit reduction of value in the last decades of life (Table 4). Many studies have suggested that estrogen may overlap the thyroid hormone action. These data taken together indicate that age-dependent depletion of estrogen may contribute to the progression of resistance to thyroid hormone action in females [16]. Thus, during a normal human life span, serum T3 is low at the time of birth, increases markedly during early infancy, remains high during childhood, is reduced after adolescence, then remains stable until late middle age, and ultimately decreases in old age [17-18]. TNYHA (New York Heart Association) functional classification states that the severity of heart disease is proportional to the decrease in T3 levels. Results of some cross-sectional studies of patients undergoing coronary angiography suggest that free thyroxin or free triiodothyronine level was inversely and thyroid stimulating hormone concentration was positively associated with the presence of CHD or the severity of coronary atherosclerosis in euthyroid subjects [19]. The relationship between variation in the mean values of the pointed hormones and genders (Table 2) expresses that a little difference among the normal rate could be observed in serum of T4 in both genders with a bit greater rate in men over 80 years than women. This information is in agreement with the previous study that in men, the value of sex hormones raises the circulating level of thyroxins binding globulin (TBG), which directly leads to an increase in the circulating level of T4 [20]. Franklyn et al., in 1985 also suggest that sex hormone status in the pre-menopausal female subject may result in an increase in TBG concentration, and in addition may have an opposing effect on circulating thyroid hormone concentrations [20]. However, somewhat contradictory results were reported by others who worked on the effect of age and gender on thyroid function and concluded that the level of T4 was higher in females than males. They further concluded that T3 and TSH levels are not influenced by gender [20]. Following findings are in accordance with the past

findings. Concerned reduction in the rate of hormones probably is in relationship with the raised T4 rate in the various life periods. While, some particular results showed who studied on the impact of gender and age on thyroid application and expressed that the greater rate of T4 in women compare to men. Then, it was demonstrated that T3 and TSH rates are not affected by gender [21]. The following research also assesses the impact of age on the various rates of TSH, APTO, T4 and, T3 which express a reduced rate of T4 in the first decade of life. It is in agreement with the previous studies. Some other same changes in T4 levels were also examined by other researchers [20]. The T3 level was shown to be raised in the first decade, that a decrease happened at first, then it increased in the later decades. This model of influence is also in accordance with the discoveries of previous researches [21]. The impact of age on the rate of TSH was seen to raise in the eighth decade in women and then reduced in the fourth decade of life in women. The rate of TSH remained nearly unaffected between the fifth to seventh decades of life in men. This model of results is in accordance with the results achieved in previous investigations [22], while some researchers demonstrated a greater TSH rate with a big raise in age item [23]. It also can be expressed that difference might be cause of this reality that the individuals in that research were not seen for any other types of disorders that may affect the tests of thyroid function. In the following study, we have chosen standard healthy-checked subjects. Hormones and TSH was assessed by some researchers and showed no changes in the rate of age and TSH [24]. TSH hormone level in women remarkably raised in the groups of over 80 years old. The enzyme thyroid peroxidase (TPO) plays a major role in thyroid hormone synthesis. Measuring the levels of anti-TPO autoantibodies is reported to be significant in diagnosing autoimmune thyroid diseases and predicting their clinical course [25]. Anti-thyroid antibodies have long been known to affect thyroid function and influence thyroid profile testing. In the following research, female between 71 to over 80 years old were the main part of the patients with high ATPO antibody

feature. In the following research, the prevalence of anti-TPO antibody in women was bigger than men, the results of Canaris et al. in 2000 came in accordance with our results that 2 to 4 times greater than males, autoimmune thyroid disorder affect females [26]. Other results have reported in a health survey in Norway, ATPO antibody prevalence was included 13.9% in females and 2.8% in males [27].These investigations are in confirmation with a greater rates of women involvement in other autoimmune disorder. Shinkov et al. concluded that among two genders existed a lot of autoimmune-related changes [28-29]. The powerful connection of thyroid disorder to malignancies of breast compared to others could be expressed by the particular relationship among these tissues. As we know, around 28% of ills who had benign fibrocystic mastopathy mostly have shown antibodies of anti-TPO as well as around 80% of them that have shown the thyroid hypertrophy issue. This is predictable that improvement in the mammary transformation of cells and improvement in the breast cancer extension both are related to oxidative stress upon iodination of proteins [30]. On the other hand, it found no influence of anti-thyroid antibodies on breast cancer survival [31-35]. It also can be one of the supplementary actions between the protection plan for other cancers and related disorders [36-45].

Conclusion

It could be concluded from the following investigation that some items like gender, age, race, and area all have a convenient impact on the levels of T4, T3,TSH, and ATPO.A major conclusion drawn from the present study is that both serum TSH and anti-TPO analyses are vital for the diagnosis of both autoimmune hypothyroidism and subclinical hypothyroidism. Moreover we need further studies to discover the link between ATPO and cancer, especially in women.

COMPETING INTERESTS DISCLAIMER:

Authors have declared that no competing interests exist. The products used for this research are commonly and predominantly use products in our area of research and country. There is absolutely no conflict of interest between the authors and producers of the products because we do not intend to use these products as an avenue for any litigation but for the advancement of knowledge. Also, the research was not funded by the producing company rather it was funded by personal efforts of the authors.

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