The Role of TSH Receptor Antibody versus Thyroid Peroxidase and Thyroglobulin Antibodies in Detecting Immune Thyroid diseases in Saudi Patients at AlmadinahAlmounawarah

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Abstract: Objective: The aim of this study was to compare role of different thyroid auto antibodies in detecting thyroid autoimmune disease and to measure the prevalence of autoimmunity in various thyroid dysfunctions in Almadinah Almounawarah, KSA. **Settings:** Madinah National Hospital in Almadinah Almounawarah. **Methods:** The study included 4 groups of subclinical- & overt hypo- and hyperthyroidism (146 cases) that were compared with 31 normal control subjects with no evidence of any thyroid dysfunction. All subjects were subjected to measurement of serum TSH, free thyroid hormones, thyroid peroxidase (TPO), thyroglobulin (TG) & TSH receptor antibodies (TSHR Abs) by the Electrochemiluminescence Immunoassay. **Results and discussion:** The study revealed that the highest prevalence of immune thyroid diseases was achieved by the dual use of both TPO and TG Abs (85.3, 83.6, 79.3 & 86.4% in subclinical hypothyroid, overt hypothyroid, subclinical hyperthyroid and overt hyperthyroid groups respectively). Slightly lower prevalence were achieved by the single use of TPO followed by single use of TG Abs. The single use of TSHR Ab revealed lower frequencies than did the previous couple, but yielded higher frequencies than that given by considering concomitant positivity of the three antibodies. Both TPO and TG correlated well with all hypothyroid cases, but the TSHR Ab correlated only with obvious clinical hyperthyroidism. Comparing mean values of antibodies in all hypothyroid versus all hyperthyroid cases gave significant differences in case of TSHR and TG Abs, but not in TPO Ab. The most differentiating antibody on comparing individual groups versus control was the TPO, followed by TG, and then lastly came TSHR Ab that showed significant difference only in both hypothyroid but not hyperthyroid groups. Comparing the 4 groups versus the control gave a highly significant difference for TPO followed by TSHR Ab. On comparing the 4 groups' together, significant differences were found between them in case of TSHR Ab. **Conclusion:** autoimmune thyroid diseases are common in Almadinah, KSA and measuring thyroid antibodies had made good characterization for autoimmunity. Dual measurement of both TPO and TG antibodies correlated well with all thyroid disorders and might has better diagnostic utility than single measurement of any of them and also was better than using TSHR Ab alone or in addition to that couple. The TSHR Ab correlated well with frank hyperthyroidism and its use should be restricted for suspicion of certain conditions. The TPO (± TG) assay appears to be more sensitive, more available and less costly than TSHR Ab assay.
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1. Introduction

The autoimmune thyroiditis is the most common cause of hypothyroidism. The role of autoimmunity is supported by the histological finding of diffuse lymphocytic infiltration of the thyroid gland and the presence of circulating thyroid auto antibodies in almost all patients. There is autosomal dominant inheritance of thyroid auto antibodies in the relatives of affected patients[(1-3)]. A polygenic basis for autoimmune thyroiditis is suggested by linkage of the disorder to several genetic loci in affected kindreds[(4)]. Autoimmune thyroiditis is more common in geographic regions of higher dietary iodine, which has been postulated to increase thyroglobulin antigenicity. However, the precise environmental factors inciting the condition remain unidentified[(5-6)].

Autoimmunity to thyroid antigens leads to two distinct pathogenic conditions with opposing clinical outcomes: hypothyroidism in Hashimoto's thyroiditis and hyperthyroidism in Graves' disease (GD). Patients with autoimmune thyroid might be hypothyroid or euthyroid; but transient thyrotoxicosis followed by hypothyroidism ("Hashitoxicosis") takes place infrequently [(7-8)]. Euthyroid individuals with autoimmune thyroiditis are at increased risk of subsequently developing hypothyroidism. The TSH receptor antibodies have been identified as responsible for indicators in autoimmune thyroid disease. These antibodies exist as stimulating in GD or blocking antibodies in hypothyroidism (neutral TRAb have been identified recently). The clinical features of GD occur when stimulating TRAb predominate. But the

relationship of TRAb to clinical phenotype and outcome is not clear when current assay methods are used. Therefore no consensus exists about its utility in diagnosing and predicting outcome in GD. The most commonly used TRAb assays, measure thyroid binding inhibiting immunoglobulins (TBII or "receptor assays") and don't differentiate between stimulating and blocking antibodies. However, the more expensive, technically demanding and less freely available "biological assays" differentiate between them by their ability to stimulate cyclic AMP or failure to do so. Failure to differentiate between TRAb types and its heterogeneous molecular and functional properties has limited TBII use to GD diagnosis and differentiating from other forms of thyrotoxicosis. The current second-third generation receptor assays are highly sensitive and specific when used for this purpose. The TRAb assays should also be done in appropriate pregnant women. Current data do not support its use in outcome prediction as there is a significant variability of assay methodology, population characteristics and study design in published data, resulting in a lack of consensus[9].

Although thyroglobulin antibodies (TG Abs) are recognized markers of autoimmune thyroid disease, they lack a defined biological action. Thyroid microsomal antibodies or anti thyroid peroxidase antibodies (TPO Abs) are found in all patients with Hashimoto's thyroiditis, in more than 70% of those with Graves' disease, and to a variable degree, in patients with non thyroid autoimmune diseases and some normal subjects. They are also established markers of autoimmune disease, and again their pathogenic role is not clearly defined. Detection of circulating thyroid auto antibodies confirms the diagnosis of autoimmune thyroiditis in patients with typical clinical presentations. Anti TPO antibodies are present in 95% of affected individuals, whereas anti TG antibodies are present in only 60% in some countries [10]. Many researches stated that TPO Ab is the most sensitive thyroid autoantibody test; and presence of this antibody has been more strongly associated with an elevated serum thyrotropin concentration than did TG Ab[11-12].

A lot of work all over the word had investigated the diagnostic role of measuring these antibodies and the prevalence of autoimmunity in different thyroid diseases but up to our knowledge, little researchers had studied this issue in the Kingdom of Saudi Arabia (KSA).

The aim of the current study was to assess diagnostic role of those antibodies and to detect prevalence of autoimmunity thyroid dysfunctions in Saudi population at Almadinah Almounawarah.

2. Materials and Methods

Subjects:

The current study involved 177 subjects that were divided into 5 groups; the first group included 31 normal subjects without any thyroid abnormality that was evidenced by normal thyroid function tests. The second group was including 34 cases with subclinical hypothyroidism, the third group included 61 patients with overt hypothyroidism, the fourth group involved 29 cases with subclinical hyperthyroidism and lastly the fifth group included 22 patients with overt hyperthyroidism. All cases were provided from outpatient clinic of Almadinah National Hospital in Almadinah Almounawarah, KSA, between March 2012 and January 2013. All groups were subjected to laboratory tests that included serum TSH, FT4, FT3, TPO Ab, TG Ab and TSH Receptor (TSHR) Ab measurements. The required ethical approvals were taken. Inclusion criteria were; all cases should be newly diagnosed adult patients, having some significant thyroid symptoms or signs. Also, cases should have biochemical evidence of thyroid dysfunction. Control subjects were clinically and biochemically normal adults. Exclusion criteria were; no children were chosen, cases under thyroid medications were excluded and control subjects with any thyroid manifestation were also excluded. No pregnant women were included in either group or also those who were receiving major medications or any hormonal therapy. The group of patients was subdivided according to TSH and thyroid hormones (FT4 and FT3) levels into subclinical hypothyroid, overt hypothyroid, subclinical hyperthyroid and overt hyperthyroid patients.

Methods:

Five ml of venous blood were allowed to clot in vacutainer tubes with serum separator. The tubes were centrifuged and serum was separated and frozen at –20 ˚C till assayed. The auto antibodies and hormones were estimated using an Electrochemiluminescence immune-assay method (ECLIA) on an automated immunoassay analyzer; Cobas e 411 from Roche (Roche Diagnostics GmbH, Sandhofer Strasse 116, D-68305 Mannheim www.roche.com). The reference ranges were primarily established as in the literature mentioned in the kit inserts. These are 0.27–4.2 µIU/ml, 12- 22 pmol/L and 3.1 – 6.8 pmol/L for TSH, FT4 and FT3 respectively, and up to 115 IU/ml, up to 34 IU/ml and up to 1.75 IU/l for TG, TPO and TSH receptor antibodies respectively [13-14].

Statistical Methods

The SPSS® (version 17) was used for data management and analysis. Quantitative data were presented as mean ± SD. For comparison of the means, the Student's t-test and ANOVA tests

were used. The Chi-square test was used for comparison of percentages. Pearson correlation was used for assessment of correlation between different variables. All tests were two tailed. ®SPSS (Statistical Package for Social Sciences)

3. Results and Discussion

All results of the current study are shown in the following tables. (*p< 0.05 was considered significant and **p ≤ 0.001 was considered highly significant).

Table (1): Sex and Age in all Studied Groups

		Sex		Age in years	
Subjects	Number	Females Number (%)	Males Number (%)	Range	Mean ± SD
Control	31	19 (61.3%)	12 (38.7%)	19- 48	27.2 ± 6.6
Subclinical hypothyroid	34	29 (85.3%)	5 (14.7%)	14 -78	38.8 ± 19.1
Overt hypothyroid	61	53 (86.9%)	8 (13.1%)	21 – 83	45.9 ± 15.3
Subclinical hyperthyroid	29	25 (86.2%)	4 (13.8%)	22- 75	42.1 ± 14
Overt hyperthyroid	22	17 (77.3%)	5 (22.7%)	18 - 67	42.4 ± 14.1
Total	177	143 (80.9%)	34 (19.2%)	14-78	---

Table (2): Comparison of Mean Values of the Three Antibodies in all Hypo- Versus all hyperthyroid Cases

Antibody	**Hypothyroid** (N=95)	**Hyperthyroid** (N=51)	**p value**
TPO (IU/ml)	249.7±208	184.2±191	>0.05
TG (IU/ml)	517.8±949	341.6±651	0.19
TSHR (IU/l)	1.6±4.3	6.4±11.3	<0.001**

When we compared all hypothyroid versus all hyperthyroid cases as regards the mean values of the three studied antibodies, a highly significant difference was found in TSHR antibody. The TSHR Ab was significantly higher in hyperthyroidism, while the mean values for the TG and TPO Antibodies were higher insignificantly in hypothyroid subjects.

Table (3): Comparison of Mean Values of TPO Ab (IU/ml)

Control N= 31	**Subclinical hypothyroid N=34**	**Overt hypothyroid N=61**	**Subclinical hyperthyroid N=29**	**Overt hyperthyroid N=22**
56.9 ± 78.7	247.1 ± 233.1**	251.2 ± 195.4**	188.9 ± 184.5**	177.8 ± 203.4*
All cases versus control[+]	p < 0.001**	p < 0.001**	p = 0.001**	p = 0.01*
All groups including control[++]	p < 0.001**			
The 4 groups of cases[++]	p >0.05			

Table (4): Comparison of Mean Values of TG Ab (IU/ml)

Control N= 31	**Subclinical hypothyroid N=34**	**Overt hypothyroid N=61**	**Subclinical hyperthyroid N=29**	**Overt hyperthyroid N=22**
86.7 ± 68.3	570.7 ± 991.9*	488.4 ± 931**	440.8 ± 844.8*	210.7 ± 161.4**
All cases versus control[+]	p = 0.008*	p = 0.001**	p = 0.03*	p = 0.002**
All groups including control[++]	p >0.05			
The 4 groups of cases[++]	p >0.05			

Table (5): Comparison of Mean Values of TSHR Ab (IU/l)

Control N= 31	**Subclinical hypothyroid N=34**	**Overt hypothyroid N=61**	**Subclinical hyperthyroid N=29**	**Overt hyperthyroid N=22**
6.6±13.5	2.3±5.7*	1.2±1.2*	4.3±10.1	9.2±12.5
All cases versus control[+]	p = 0.045*	p = 0.03*	p >0.05	p >0.05
All groups including control[++]	p = 0.002*			
The 4 groups of cases[++]	p < 0.001**			

[+] Post-hoc [++] ANOVA test

When we compared all groups versus the control group as regards the three antibodies, the mean values for both TPO and TG Abs in all patients' groups were significantly higher than those in the control group. In doing the same for TSHR Ab, the mean values in the two groups of hypothyroidism (both subclinical and overt) were significantly lower than that in the control, but no significant differences were shown between the control group and any of the hyperthyroid groups. This might be attributed to the fact that in the control group, there were few persons having very high levels for TSHR Abs that affected

the mean (if those persons were allowed to be followed up, they might develop thyrotoxicosis later in life). On comparing the 5 groups (including the control), the best differentiating antibody was the TPO, followed by TSHR and no significant difference was found in case of TG Ab. But on comparing the 4 groups of patients together and excluding the control from this comparison, a significant difference was only shown in case of TSHR Ab.

Table (6): Antibodies with Significant Correlations

Variables	Pearson Correlation Coefficient	p value
TPO & TG Ab	0.3**	<0.001
TPO Ab& TSH	0.26**	<0.001
TG Ab& TSH	0.29**	<0.001
TSHR Ab& FT4	0.35**	<0.001
TSHR Ab& FT3	0.46**	<0.001

From the correlation study, it was concluded that both TPO and TG Abs correlated significantly and positively together and also with TSH which is the single sensitive test for early diagnosis of subclinical thyroid disorders. And since TSH usually increases in all hypothyroid disorders whether subclinical or overt, we can say that both TPO and TG Abs correlated well with hypothyroidism. Also, there was significant positive correlation between TSHR Ab and both thyroid hormones (FT4 & FT3) that are late diagnostic parameters for thyroid dysfunctions and only they increase in obvious clinical hyperthyroidism. Thus, the TSHR Ab correlated well with only frank hyperthyroid disorders.

Table (7): Frequency of Positive Cases for Auto Abs in Each Group as Compared by Control Group

Positive Cases for Antibody	Control	Subclinical Hypothyroid	Overt Hypothyroid	Subclinical Hyperthyroid	Overt Hyperthyroid
TSHR Ab	**29%**	**14.7%**	**18%**	**31%**	**68.2%**
p value	**--**	**>0.05**	**>0.05**	**>0.05**	**<0.05***
TPO Ab	**22.6%**	**73.5 %**	**80.3 %**	**69 %**	**77.3 %**
p value	**--**	**< 0.001****	**< 0.001****	**= 0.001****	**< 0.001****
TG Ab	**19.3 %**	**67.6 %**	**62.3 %**	**65.5 %**	**77.3 %**
p value	**--**	**< 0.001****	**< 0.001****	**< 0.001****	**< 0.001****
Any of TPO or TG Abs	**29%**	**85.3%**	**83.6%**	**79.3%**	**86.4%**
P value	**--**	**<0.001****	**<0.001****	**<0.001****	**<0.001****
TPO, TG & TSHR Abs	**9.7%**	**2.9%**	**13.1%**	**24.1%**	**45.5%**
p value	**--**	**>0.05**	**>0.05**	**>0.05**	**0.004***

The positive correlation between TPO and TG Abs in table 6 let us ask an important question that was: is this couple of antibodies or even that profile sufficient for detecting autoimmune thyroid disease? Or does the TSHR Ab assay add any new beneficial data if it is added to the previously mentioned couple? To answer these questions we calculated the percentage of positive subjects for one of or both of TPO and TG Abs in each group and compared it with percentage of positive subjects for TSHR Ab. Comparison also included subject's positive for the presence of the three antibodies together. We found that the use of the previous couple of TPO and TG Abs whether we considered both of them or any one of them was too much better in detecting autoimmunity than did the TSHR Ab whether we were looking for it per say or its presence with the other antibodies. This means that TSHR Ab assay did not add much in detection of autoimmunity in thyroid diseases, whether it was done alone or in conjunction with the couple of TPO and TG Abs. Only it might be of some value in detecting autoimmune hyperthyroid disease.

Some authors recommended the use of TSHR Ab only on certain occasions like the diagnosis of clinically (not biochemically) suspected Graves' disease or for monitoring therapy, predicting remission or predicting fetal disease in pregnant women [15-18].

The TSHR autoantibodies may be detected before autoimmune thyrotoxicosis becomes biochemically or clinically manifest. Since none of the treatments for Graves' disease are aimed at the underlying disease process, but rather ablate thyroid tissue or block thyroid hormone synthesis, Thyroid Stimulating Immunoglobulin (TSI) may persist after

apparent clinical cure. This is of particular relevance for pregnant women with a history of Graves' disease that was treated with thyroid-ablative therapy. Some of these women may continue to produce TSI. Since TSI are IgG antibodies, they can cross the placental barrier causing neonatal thyrotoxicosis [15-17]. While the gold standard for thyroid-stimulating immunoglobulins is the bioassay, the thyrotropin receptor antibody test has a shorter turnaround time, less analytical variability, and is less expensive than bioassay, but yet it is less available in routine laboratories and more expensive than TPO and TG Abs.

The thyroid studies focused on iodine deficiency as the most important cause for thyroid dysfunctions in the twentieth century. Following introduction of iodized salt and iodine in other foods, iodine deficiency was eliminated in most countries [19-22]. Nowadays, thyroid diseases are related to other acquired causes, many of which are worsened by excessive iodine intake [23]. This is why it is essential to identify or exclude autoimmunity before giving any iodine supplements which can improve the condition if it is due to iodine deficiency but unfortunately will exacerbate it if autoimmunity is the cause of dysfunction. Because the thyroid dysfunctions are common in KSA, it is crucial to test for thyroid auto antibodies aiming at detecting the most common cause responsible for pathogenesis of thyroid dysfunctions in Saudi population and to provide an approximate frequency for autoimmune thyroid disorders in this community. The current work reported that the autoimmune thyroid diseases are very common in Almadinah, KSA (table 7). The dual measurement of both serum TSH and thyroid auto antibodies is essential for evaluation of thyroid status particularly subclinical thyroid diseases. Single measurement of TSH might overlook the diagnosis of subclinical autoimmune thyroid disease. Also detection of autoimmunity as a cause of thyroid dysfunction is a must in order to avoid the miss use of excessive iodine that may aggravate the autoimmune thyroid disease. Dual measurement of both TPO and TG antibodies has better diagnostic utility than single measurement of any of the three studied antibodies.

From the previous results, we can say that the measurement of TPO antibody could be considered more superior to both TG and TSHR antibodies in detecting immune thyroid diseases. But we noticed that combination of both TPO and TG antibodies gave much higher frequencies when compared by using any one alone or doing them all together. This means that, although the TPO could be considered better for detecting autoimmunity, but the use of both TPO and TG antibodies will help to minimize ignoring autoimmunity as an etiological factor for the thyroid dysfunction. The current prevalence was in agreement with other investigators who reported close figures in subclinical and overt hypothyroidism, but they did not work on hyperthyroid cases [24]. In a study made in Aseer, KSA, frequencies for microsomal TPO antibodies were ranging from lower figures as 12.5% in diffuse simple goiter which is not associated with altered hormone levels i.e. euthyroid (resembles biochemically the control group) and also 28% in multinodular goiter (sometimes euthyroid) to higher percentages as 69% in hypothyroidism and 75% in toxic goiter (hyperthyroidism). In that work, they did not measure the TSHR Ab but they measured the Thyroid Binding Inhibitory Antibody (TBI Ab) which was positive in 28.7% of their patients. This means that it was lower than TPO Ab. They also recommended the use of TBI Ab assay for monitoring recently diagnosed Graves' disease and they considered it a good predictor for relapse in patients taking anti thyroid drugs. They also recommended the dual use of TPO Ab and TSH tests for initial assessment of suspected hypothyroidism and primary toxic goiter. The previous figures agreed with our results to a great extent, but they classified their patients by surgical classification, not functional classification as we did [25]. Another study was made in Riyadh, KSA that reported lower frequencies for TPO antibodies that were; 58% for goiter, 50.4% for hypothyroidism and 30% for hyperthyroidism [26].

A research was made in Jeddah on subclinical hypothyroid cases only, and the authors recorded a percentage of 61% for cases positive for TPO antibodies which was lower than the frequency in our cases (73.5%). The difference may be attributed to the difference in methodology as we used one of the most sensitive and specific assay that was electrochemi-luminescence immunoassay, but the researchers in Jeddah used the indirect hemagglutination assay that has lower sensitivity and detection limit than does the current technique. On the other hand, the close figures in the study made in Aseer may be attributed to their use of a sensitive and specific radioimmunoassay method [25]. Other reports recorded frequencies ranging from 20 to 78% [27-30]. Care should be taken when interpreting results for thyroid antibodies as the case might be pregnant or at post partum period and this could affect the result of thyroid auto antibodies. Another research was done in Riyadah, KSA that recorded frequencies for TPO antibodies in normal pregnant females that were 4.3%, 4.9% and 3.5% at the post partum period (4-6 weeks, 6-8 weeks and 8-12 weeks post partum respectively). At the same period they recorded frequencies for TG antibodies that were 2.9%, 1.2% and 1.4% respectively, but with follow up there was no clinical evidence for

developing hypo or hyperthyroidism in any of their subjects [31].

In certain district in China, some researchers reported the following frequencies; 94.6%, 76.3% and 20.4% for TPO, TG and TSHR antibodies in Hashimoto's thyroiditis (hypothyroidism) and 40%, 30% and 90.3% for Graves' disease (hyperthyroidism) [32]. These results are slightly higher than our results as regards the hypothyroid patients, but their results are too much lower than ours in case of hyperthyroidism. The difference may be related to the geographical difference and also to a local public health problem of iodine deficiency that is much more apparent at that district in China [33]. Currently available information suggests that multiple genes with modest association to auto- immune diseases contribute to susceptibility to these disorders. Also, the associations may differ for the various ethnicities [34].

In the Whickham follow-up study, women with thyroid auto antibodies (11% of the population) had an eight fold higher likelihood of developing overt hypothyroidism over 20 years than did antibody negative women [35]. In women with both thyroid auto antibodies and isolated thyrotropin elevation, the risk of progression to overt hypothyroidism was 38 times higher, with a 4% annual risk of developing overt hypothyroidism [6, 36]. A reference study (NHANES III) [37] was done in the US on a sample of 17,353 people aged >12 years representing the geographic and ethnic distribution of the U.S. population. A disease free population of 16,533 people was selected from the previous sample and a further reference population of 13,344 people was selected from the disease free population by excluding, in addition, those who were pregnant, taking androgens or estrogens, who had thyroid antibodies, or biochemical hypothyroidism or hyperthyroidism. They concluded that the prevalence of antithyroid antibodies are greater in females (in disease free population), increase with age, and are greater in whites and Mexican Americans than in blacks when compared with their reference population. The TG Ab alone in the absence of TPO Ab is not significantly associated with thyroid disease in their study. The lower prevalence of thyroid antibodies and lower TSH concentrations in blacks needed more research to relate these findings to clinical status [37]. This means that ethnicity plays a role in prevalence of autoimmunity in that defined community.

In one of the most comprehensive systematic review of autoimmune thyroid disease conducted in the past two decades, the best estimates of the incidence of hypothyroidism was 350/100 000/year in women and 80/100 000/year in men; the incidence of hyperthyroidism was 80/100 000/year in women and 8/100 000/year in men [38]. To compare their results with figures in KSA, a large reference prospective study should be done on the Saudi population that should include all age and ethnic groups and most geographic areas. Long follow up (for years) may give more accurate figures for incidence of autoimmune thyroid diseases in KSA. This considerable variation in the frequency and distribution of thyroid antibodies in the available researches may be due to the variations in techniques of detection, definition of abnormal titers, and inherent differences in the populations tested. By using a competitive immunoassay procedure, the reported prevalence of detectable TG Ab and TPO Ab levels were 10% and 12% of the healthy population. A hypoechoic ultrasound pattern or an irregular echo pattern may precede TPO Ab positivity in autoimmune thyroid disease, and TPO Ab may not be detected in more than 20% of individuals with ultrasound evidence of thyroid autoimmunity [39]. A recent research has confirmed an association between TPO Ab levels and gene polymorphism [40].

Early post-mortem studies confirmed histological evidence of chronic autoimmune thyroiditis in 27 % of asymptomatic adult women, with a rise in frequency over 50 years, and 7 % of asymptomatic adult men, and diffuse changes in 5 % of women and 1 % of men [41]. This might explain the presence of auto antibodies in some of our control subjects. It is crucial to detect patients with high antibodies titers especially if they are elderly patients with subclinical hypothyroidism as they may have higher than previously recognized risk of rapid development of overt hypothyroidism. More frequent thyroid testing and follow up (with shorter interval than that recommended by most professional guidelines) may be needed. The early recognition and intervention with levo-thyroxine treatment may be indicated and prevent serious complications [42]. Also, high TPO Ab is associated with poor physical and psychological well-being and appears to predict future health perception in Hashimoto's thyroiditis patients [43]. Lack of vitamin D was suggested as a predisposing factor to autoimmune diseases, and was shown to be reduced in patients with thyroid autoimmunity. In turn, its deficiency is also linked to infertility and pregnancy loss, suggesting a potential interplay with thyroid autoimmunity in the context of infertility. In addition, thyroid auto antibodies were also suggested to alter fertility by targeting zonapellucida, human chorionic gonadotropin receptors and other placental antigens [44]. All these data adds to the necessity of identifying autoimmunity in thyroid disorders.

In conclusion, autoimmune thyroid diseases are common in Almadinah, KSA and measuring thyroid

antibodies had made good characterization for autoimmunity. Dual measurement of both TPO and TG antibodies correlated well with all thyroid disorders and might has better diagnostic utility than single measurement of any of them and also better than using TSHR Ab alone or in addition to that couple. The TSHR Ab correlated well with frank hyperthyroidism and its use should be restricted for suspicion of certain conditions. The TPO assay alone or with TG assay appeared to be more sensitive, more available and less costly than TSHR Ab assay.

Recommendations

A wider reference prospective study should be done on the Saudi population that should include all age and ethnic groups and most geographic areas. Better sampling methodology that considers regional differences could represent well the KSA. Long follow up for normal subjects with high antibody levels may give more accurate figures for incidence of auto immune thyroid diseases in KSA. Also, monitoring therapy and re-measuring of the antibodies might improve the prognostic value of testing these antibodies.

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