RESEARCH STUDY

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Serological and histopathological study of thyroid diseases, prospective study

Article Information

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Abstract

Background: Accurate detection of thyroid autoantibodies by enzyme linked immunosorbant assay technique namely thyroglobulin antibody, thyroid peroxides antibody is crucial in the differentiation of autoimmune thyroid disorders from other form of thyroid diseases.
Objective: Evaluation of the detection of thyroglobulin antibody and thyroid peroxides antibody in different thyroid diseases using enzyme linked immunosorbant assay technique.
Methods: - Seventy-five patients admitted to Surgical Units of Baghdad Medical City Hospital for the period between "October 2010 to June 2011" they were waiting to do thyroidectomy. They were chosen nonselectively for serological evaluation of above autoantibodies , and correlation of the results with histopathological diagnosis.
Results:- Clinical results; Colloid goiter is common cause of hyperthyroidism (19 were colloid goiter out of 30 total hyperthyroid patients) (63%) , and still common thyroid surgery (56 were colloid goiter out of 75 thyroid surgery) (75%).
Histopathological results;- 56 cases (75%) had colloid goiter, 9 patients had Graves' disease (12%), and 3 had lymphocytic thyroiditis (4%), 7 had thyroid neoplasia (both benign and malignant) (9%).
The serological results; Antibodies positive results were 6 patients (10.7%) in colloid goiter (p-> 0.05), 6 patients (66%) and 1 patient (33%) for GD, and lymphocytic thyroiditis respectively(P-< 0.05)., while its all were negative in thyroid neoplasia.
Conclusion:- Serum thyroid autoantibodies determination is valuable test in clinical practice of autoimmune thyroid diseases.

Introduction - Goiter occurs to some degree almost every country of the word making no distinction of race, nationality or color [(1)] . In spite of preventive measures of endemic goiter which has been introduced in Iraq, such as the use of iodized salt, thyroid specimens still constitute considerable number of biopsies received in histopathological laboratory [(2)]. Clinicians have been paid a little attention to the goiters induced by autoimmune mechanism in the management of thyroid diseases. Although in Iraq hyperthyroidism arises from endemic goiter form 60% of total cases of thyrotoxicosis, the autoimmune mechanism still cause hyperthyroidism in considerable percentage [(3)]. Accurate detection of thyroid autoantibodies (Tabs) by enzyme linked immunosorbant assy (Elisa) is crucial in the differentiation of autoimmune thyroid disorders from other form of thyroiditis, in addition to that TAbs are useful immunological markers in the diagnosis, management and follow up of different types of autoimmune thyroid diseases (AITD) [(3)]. The presence of TAbs is associated with an increased risk of unexplained subfertility [(4)].

Methods: - Seventy five patients admitted to the surgical unit of Baghdad Medical City hospital for the period between October 2010 to June 2011 were chosen nonselectively for evaluation. The patients were suffering from different thyroid diseases and they were waiting for doing thyroidectomy. They were submitted to following procedures:-
Serological.
Histopatlogical.
1-Serological evaluation:-Five-ml venous blood samples were obtained preoperatively from all the above patients, the blood allowed clotting naturally at room temperature, and then sera were separated after centrifugation at 1500 vpm for 5-10 minute. Heamolysis was avoided. The serum kept in plastic plain tubes, each sample was labeled by a serial number & patient's name. Then the sera were frozen at -20° c.
At proper time all stored serum sample are thawed then examined using enzyme linked immunosorbant assay (Elisa) for evaluation of:
Serum thyroglobulin Ab (Tg Ab)
Serum thyroid peroxidase Ab (TpoAb)

2- Histopathologiocal evaluation: - The thyroid specimens were examined grossly and carefully sectioned, few represented sections were done, these underwent the classical processing method to obtain finally the paraffin embedded tissue sections (blocks).

Methods: - Two main techniques were used in the present work namely serological, and histopathological.

1. Serological tests by Elisa using Kallestad microplate Eia kit [5].

All stored serum of patients are thawed and subjected to the following serological test.

1. Determination of Tg Ab.
2. Determination of Tpo Ab.

All specimens are formaldehyde fixed, paraffin embedded, sectioned at 3-5 microns, mounting of the specimen on glass slides.

Results:-Could be divided into clinical, histopathological, and serological.

Clinical: - This part includes the study of 75 patients suffering from different thyroid diseases. It includes 59 females and 16 males. F/M ratio is 3.7/1. Age range is 14-66 years, mean age (40 years $\pm$ 12.1).

There is predominance high female/male ratio in all thyroid diseases.

A total of 30 patients with hyperthyroidism were found, they are 19 cases of colloid goiter (multinodular toxic goiter) (MNTG), 9 patients with GD & two with (LT). So MNTG constituted the most common cause of hyperthyroidism in Iraq, it represent 63% of hyperthyroidism.

Regarding thyroid surgery in general colloid goiter represent 74% of all thyroid surgery.

Histopathological: - Table 1

Serological:-Thyroid autoantibodies namely TgAb and TpoAb are evaluated.

Table 1 summerized the result.

Table-1: Clinical, histopathological, and serological findings

	Colloid Goiter	Graves' disease	Lymphocytic thyroiditis	papillary Carcinoma	Anaplastic Carcinoma	Follicular Adenoma	Total
Age range	20-66	14-43	20-30	35-60	56-64	25-35	
Female	42	8	3	3	2	1	59
Male	14	1	-	-	-	1	16
Toxicity	19	9	2	-	-	-	30
+ve Tg Ab	5	4	1	-	-	-	10
+ve TPO Ab	4	5	-	-	-	-	9
+ ve both Abs	3	3	-	-	-	-	5
Total Abs	6	6	1	-	-	-	13
Number of patient	56	9	3	3	2	2	

The percentages of antibodies in different groups of diseases are as follow:

Antibody results in GD are positive in 6 patients from total number of 9 patients (66%). LT 1 patient was positive out of 3 (33%), While 6 only are positive in CG from a total of 56 patients (10.7%).

The serological result is statistically significant in cases of GD and LT with P-value less than 0.05 & a statistically not significant in cases of CG (Table 2).

Table2: significance of positive thyroid autoantibodies findings

	Graves disease and lymphocytic thyroiditis N=12	Colloid Goiter N=56
No. of +ve Ab	7	6
P-value	< 0.05 (sig.)	> 0.05 (Not sig.)

Discussion:-

Clinical

• MNTG represent 63% of toxic goiters, this agrees with *Adel M.A* & *Aga Azaim K*1993 who stated this figure as being 60% in Iraq [3].

• Thyroid surgery: In general CG represent 74.6% of all types of thyroid diseases undergo surgery, this finding is slightly lower than that found by *Al-Hadithi W* & *Al-Hashimi AS* 1985[1] who stated that colloid goiter represented 82% of total thyroid surgery, and this may be due to dropping in cases of CG as result of preventive measures of dietary iodine deficiency.

The predominant high F/M ratio in thyroid diseases could be due to pregnancy, lactation or sex hormones.

2. Serological

Elisa technique was applied in the present work for the determination of TgAb & TpoAb.

Regarding simple goiter; *Roitt et al* 1985 found 27% of simple goiter has Ab in their sera, *Doniach et al* 1960 found 33%, Anderson 1967 found 20%, *Zweiman* & *Lisak* 1979 found 20-30%

while *Men & Kriss* used sensitive Radioimmunoassy (RIA) found that 11% of patients with simple goiter have Abs [6]. Our results are slightly lower than that found by *Yasso et al* 1989 who found 16-17% of patients with simple goiter have Abs [6] .The higher results of other authors may be due to lack of sensitivity of the method used.

All our nineteen patients of MNTG were -ve for antibodies while it should follow simple goiter in the percentage of Abs, this can be explained by the role of antithyroid therapy prior to surgery in this group of patients.

Among patients with Graves' disease (GD), and lymphocytic thyroiditis(LT), this work demonstrated TAbs range from 33-66% in GD which is in agreement with *Caron P et al* 1991, *Foldes I & Levay A* 1994 [7,8],and *Dham, Anand et al* 1995 in India[9]. But disagree with *Nakamura H et al* 1991 in Japan[10] and *Tayyab M* et al 1997 in Pakistan[11], and several recent studies[12-15] which found higher figures approaching 90%. The differences could be attributed to the use of antithyroid drugs prior to surgery; method applied for estimation of Abs, & could be due to geographical differences.

It should be mentioned here that viral infections can leads to increase level of Ab in blood *(Scharbaum WA* 1987) [16]. So it should be considered in higher results.

The 7 cases of thyroid adenoma and carcinoma are negative for Abs. This small number of patients was insufficient to confirm the findings.

The relationship between malignant thyroid diseases and AITD had been confirmed by *Spencer CA et al* [17, 18], they showed that patients with differentiated thyroid carcinoma (DTC) have 3 folds thyroid autoantibodies in their sera more than normal subjects.

Conclusion: - Serum thyroid autoantibodies determination is valuable test in clinical practice of AITD, and it correlate with the activity of the disease and response to anti thyroid drugs.

References:-

1. Al-Hadithy WK, Al-Hashimi AS, Al-Saleem TI. Pathology of thyroid gland in endemic goiter and possible relation to malignancy, a clinicopathological study. M.Sc. Path. Thesis Baghdad University 1986.

2. Ibrahim KS, Al-Mukhtar MY, Al-Sakkal NS. Surgical pathology of thyroid diseases in the northern part of Iraq.J. Fac. Med. Baghdad 1988 Volume 30.No. 4.403-10.

3. Adel M.A, Aga Azam K. Toxic goiter incidence, clinical feature, and post-operative complication, to FICMS. Surg. Thesis 1993.

4. Van Den Boogaard, E.; Vissenberg, R.; Land,J.A.; Van Wely,M.; Van Der Post,J.A.;Goddijn,M.; Bisshop, P. H. (2011). " Significance of (sub) clinical thyroid dysfunction autoimmunity before conception and in early pregnancy: A systemic review. *Human Reproduction Update 17* (5):605-19.

5. Kallestadantithyroglobulin (Tg) microplateEia and Kallestad. Antithyroglobulin (Tg) microplate. Antithyroid peroxidase (Tpo) for the qualitative or semi quantitive detection of IgG autoantibodies specific for (Tg) or for (Tpo) in human serum or plasma by indirect enzyme immuno assy. Chaska sanof: diagnostics Pasteur. Inc. 1996.USA.

6 .Yasso B.M.R, Al-Nasiry S.A, Al-Hashimi A.S. Immunologic aspect of thyroid diseases. M. Sc. Thesis 1989.

7 . Caron P et al. Antithyroid peroxidase in non neoplastic thyroid pathology. Rev. Med. Interne. 1991 Sep-Oct; 12(15):335- 38.

8. Foldes I, Levay A: Antibodies -against thyroid gland peroxidase and thyroglobulin in various thyroid diseases. Orv. Hetil 1994. Jul. 17:135(29): 1979-1584.

9. SK DHAM, AC Anand G. Dhananjayan. Microsomal and thyroglobulin antibodies in thyroid disorders MJAFI (medical Journal Armed Forces of India). 1995: 51: 247-50.

10. Nakamura H, Mikami Y, Aono Y. Measurement of anti microsomal and antithyroglobulin antibodies by radioimm-unoassay. Rinsho-Byori. 1991 Apr. 39(4):373-79.

11. Tyyab M. Ditta A, Malik A.M., et al. Significance of thyroid microsomal antibody in Graves' disease. JPMA 1993:Vol 43:No.I.

12. Utiger, editors, Lewis E. Braverman, Robert D. (2005). *Werner & Ingbar's the thyroid : a fundamental and clinical text* (9th ed.). Philadelphia: Lippincott Williams & Wilkins.

13. Chardès T, Chapal N, Bresson D, Bès C, Giudicelli V, Lefranc MP, Péraldi-Roux S (June 2002). "The human anti-thyroid peroxidase autoantibody repertoire in Graves' and Hashimoto's autoimmune thyroid diseases". *Immunogenetics* 54 (3): 141-57.

14. McLachlan SM, Rapoport B (2000). "Autoimmune response to the thyroid in humans: thyroid peroxidase--the common autoantigenic denominator". *Int. Rev. Immunol.* 19 (6): 587-618.

15. Ai, J; Leonhardt, JM; Heymann, WR (2003 May). "Autoimmune thyroid diseases: etiology, pathogenesis, and dermatologic manifestations". *Journal of the American Academy of Dermatology* 48 (5): 641-59; quiz 660-2.

16. Scherbaum W.A. On clinical importance of thyroid microsomal and thyroglobulin antibodies determination.Acta.Endocrinol (copenh) 1987: Suppl:281.

17 .Spencer C.A et al, Serum thyroglobulin autoantibodies prevalence influence on serum thyroglobulin measurement, and prognostic significance in patient with differentiated thyroid carcinomas. J. Clin. Endocrinolmetabol. 1998 Apr: 83(4): 1121-7(abst).

18. Spencer CA, Clinical utility of thyroglobulin antibody (TgAb) measurements for patients with differentiated thyroid cancers (DTC).
.J Clin Endocrinol Metab. 2011 Dec; 96(12):3615-27. Epub 2011 Sep 14.