

Study of some aspects of autoimmune response for patients of thyroiditis

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Abstract: A study were performed to estimation the concentrations of the hormones (T3, T4 and TSH) , thyroglobulin(Tg) and thyroid peroxidase (TPO) aut antibodies , and the concentration of HLA-DR alleles in patients with thyroid diseases in Babylon province .The study reveals that the T4 levels were significantly increased ($p < 0.05$) in hyperthyroidism patients compared with other groups and healthy subject , also there is a significant increased ($p < 0.05$) in TSH level in hypothyroidism group compared with other groups; furthermore , the concentration of TPO auto-antibody show highly significant elevation ($p < 0.05$) in hypothyroidism and hyperthyroidism patients compared with other group and healthy individuals . Meantime , there is significant differences ($p < 0.05$) in TG auto-antibody between hyperthyroidism patients and other groups ;while there were significantly increased ($p < 0.05$) in frequency of HLA-DR alleles in all groups of patients compared with healthy subjects , furthermore , the results reveals increased ratio of disease in females compared with males , also the ratio of thyroiditis patients were higher in second age categories compared with first and third age categories .

Key words: Autoimmunity . Graves' Disease Hashimotos' Thyroiditis . HLA-DR Alleles

I. Introduction:

The immune response to self antigens or antigens associated with the commensal microbiota are called autoimmunity and can lead to autoimmune diseases that are characterized by tissue damage (Janeway et al.,2005 ; Kenneth et al.,2012). In organ-specific diseases , autoantigens from one or a few organ only are targeted , and disease is therefore limited to those organs for examples of organ specific autoimmune diseases are Hashimotos' thyroiditis and Graves' disease , both predominantly affecting the thyroid gland (Harveg and champe,2008). The mechanism of Graves' disease characterized by production of auto antibodies against the thyroid-stimulating hormone receptor(TSHR), and the consequences is hyperthyroidism which means overproduction of thyroid hormones(T3,T4 and TSH) (Jack ,2002 ; Hasham & Tomer , 2012) , moreover this disease is discovered mostly in the third and fourth decades of life (Klein & levey,2000).The Hashimotos' disease was represented by production of thyroglobulin (Tg) , thyroid peroxidase (TPO) autoantibodies and autoreactive Tcells against thyroid antigens ,and the results is destruction of thyroid tissue leading to hypothyroidism (underproduction of thyroid hormones) (Burmester & Pezzmtto, 2003 ; Pandiyan , 2011) .Studies have shown the existence of power correlation between HLA gene and its specific autoimmune disease and this is expressed by relative risk , in addition, there is a different in the recurrence of HLA-DR alleles in patients with thyroiditis within population groups according to the ethnicity and geographic location (Harvey & Champe,2008 ; Ban , 2012). Therefore, the aim of this study to determine the proportion of disseminate of these diseases by evaluate certain autoantibodies, hormones and HLA-DR alleles ,as well as their relationship with age and sex, also to knowledgment the correlation between thyroiditis with environmental and genetic factors in Babylon province .

II. Materials and Methods:

1- Patients and Control:

The work was applied on 60 patients of thyroiditis (12 males and 48 females) admitted to the Teaching Hilla hospital and General Mahaweel Hospital in Babylon province , and 21 apparently subject (7 males and 14 females) with no symptoms of thyroiditis were selected as control group. Patients were classified into four subgroups :Hyperthyroidism (20 patients) , Hypothyroidism (20 patients) , Euthyroidism (10 patients) and Family history (10 patients), while the cases of this study were divided into three age categories for comparison:(6-25) , (26-45) and (46-65) years . The number of cases was 15 , 31 and 14 in each category respectively .

2- Blood Samples:

The blood samples were drawn from each patients and control (5ml) by vein puncture using disposable syringes . The blood was placed in the Jel tube and kept to clot at room temperature (25-20) ° C , then centrifugated at 3000 rpm for 10 minutes after that sera samples were carefully transferred to appendorf tubes and preserved at -20° until use (Bishop et al ., 2000)

3- Tests:

A- Hormonal Tests :

The concentration of the hormones T3, T4 and TSH were estimated by cobas e 411 according to the automatic procedure of Roche Hitachi company (French).

B- Immunological Tests :

1- The concentration of anti –thyroid peroxidase (TPO IgG) and anti – thyroglobulin (TG) were estimated by ELISA according to the manual procedure of DAI company (USA) .

2- The frequency of HLA-DR allele was estimated by ELISA according to the manual procedure of DAI company (USA) .

4- Statistical Analysis :

The results were analyzed using statistical system SPSS version -17 (T-testing and ANOVA-LSD-General Linear Model) .

III. Results:

The result showed that the ratio of patients with thyroiditis were higher in females compared with males in all age categories , which reached 66.67, 87.1 and 78.57 % in the first , second and third age groups respectively , while this ratio in males were. 33.33, 12.9 and 21.43 % consuctively (figure 1).

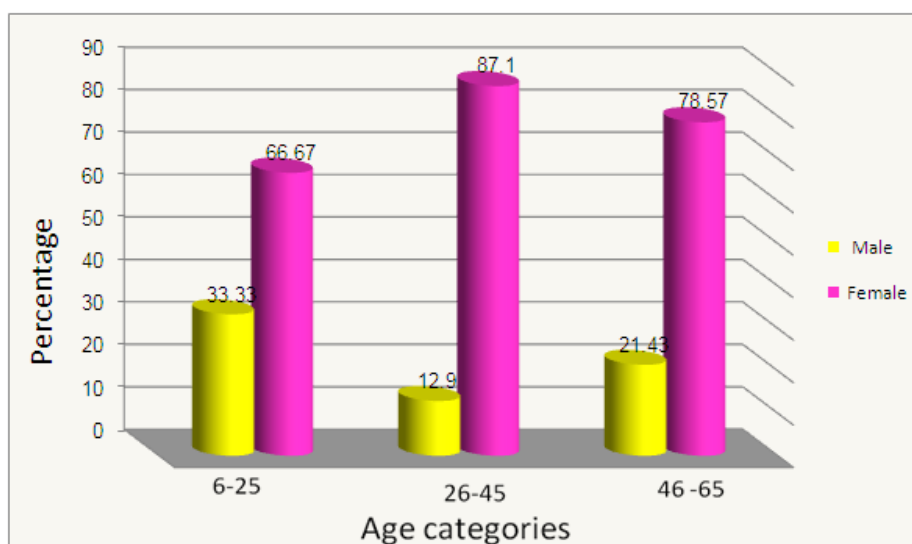


Figure (1): The relationship between sex and patients with thyroiditis of different age categories .

The results illustrated that there was significant differences ($p < 0.05$) in mean of concentration of T4 hormone in the hyperthyroidism patient when compared with other subgroups of patients and healthy individuals, while the concentration of TSH hormone were increased significantly ($p < 0.05$) in the hypothyroidism subgroup when compared with others , as well as there were significant differences in mean of concentration of autoantibody TPO in hyperthyroidism and hypothyroidism subgroups when compared with others groups . In addition the level of autoantibody TG was increased significantly ($p < 0.05$) in patients with hyperthyroidism when compared with patients and control groups.

The mean level of HLA-DR3 alleles showed significant differences ($P = < 0.05$) in hypothyroidism patients when compared with hyperthyroidism, Euthyroidism subgroups and the control group, furthermore they revealed significant difference in the level of this allele in Family history patient , when compared with hyperthyroidism , Euthyroidism and a healthy individuals groups , as illustrated in table (1).

Table (1): The concentrations of hormones (T3,T4 and TSH) , autoantibodies (TPO and TG) and HLA-DR3 in patients with thyroiditis .

Groups Parameters	Control Mean \pm S.E N=21	Hyperthyroidism Mean \pm S.E N=20	Hypothyroidism Mean \pm S.E N=20	Euthyroidism Mean \pm S.E N=10	Normal genetic S.E \pm Mean N=10	L.S.D
T3 nmol/L	1.82 \pm 0.11	3.74 \pm 0.43	1.11 \pm 0.16	1.88 \pm 0.13	2.13 \pm 0.16	1.76
T4 nmol/L	98.19 \pm 3.15	159.94 \pm 9.62	72.12 \pm 6.87	104.6 \pm 4.63	103.30 \pm 4.41	36.41
TSH μ IU/ml	2.04 \pm 0.21	0.16 \pm 0.11	37.81 \pm 4.03	2.49 \pm 0.74	1.68 \pm 0.49	10.84

TPO IU/ml	6.73±1.57	28.59* ±8.06	29.99*±5.42	8.25 ±2 .05	14.35± 3.41	13.37
TG IU/ml	0.45±0.16	25.29*±5.83	8.73±2.43	0.78± 0.24	1.45± 0.72	11.53
HLA-DR3 IU/ml	12.55±0.79	16.64± 1.35	22.33±2.10	17.46± 2.29	21.24± 2.72	3.8

there was an elevated number of patients in the first and second age groups of Hypothyroidism, which reached 10% (6 patients) and 18.33% (11 patients) respectively, while the number of patients with hyperthyroidism was increased in the third age group that reached 11.66% (7 patients), as revealed in table (2).

Table (2): The relationship between age and thyroiditis patients.

Age category (years)	Groups Of patients	Number of Patients	Percentage%
6-25	Hyperthyroidism	4	6.67%
	Hypothyroidism	6	10%
	Euthyroidism	1	1.67%
	Family history	4	6.67%
26-45	Hyperthyroidism	9	15%
	Hypothyroidism	11	18.33%
	Euthyroidism	5	8.33%
	Family history	6	10%
46-65	Hyperthyroidism	7	11.66%
	Hypothyroidism	3	5%
	Euthyroidism	4	6.67%
	Family history	0	0.00%
Total Number		60	100%

IV. Discussion:

The results showed that the ratio of incidence increased in females compared with males in all age groups. Fairweather, (2007) & Kumar et al., (2013) reported that a high frequency of disease in women when compared with men (Muhammad, 2009; Ali et al., 2002; Bjoro et al., 2000; Ahmed et al., 2004). Thyroid disorders are prevalent worldwide, especially in women, and this is associated with sex hormones and the X chromosome which affect the thyroid and immune system (Lichiardopol & Mota, 2009).

The study showed a highly significant increase in concentration of T4 hormone in patients compared with other groups. Choski et al., (2003) & Devi et al., (2012) revealed that hyperthyroidism increases the effectiveness of tissue within the thyroid gland, which results in hyperactivity in the production of one or both thyroid hormones (T3 and T4), and he reported that most causes of hyperthyroidism was Graves disease (GD) which is an autoimmune disease where the antibodies to the thyroid stimulating hormone receptor (TSHR) makes the thyroid gland produce too much hormone. The sera of patients with hypothyroidism showed higher values of the hormone TSH in comparison with other groups. Mansoor et al., (2011) reported that a decrease in the effectiveness of the thyroid gland, leading to a rise in the level of the hormone TSH to more than 10 µ IU/ml. Results revealed a significant difference in level of auto-antibodies TPO to the thyroid gland in the hypothyroidism and hyperthyroidism groups in comparison with other groups. The patients with hyperthyroidism showed higher values of serum TG-Ab compared with other groups. The autoantibodies for TG and TPO were regarded as markers to the autoimmune thyroid diseases, in which TG-Abs were higher prevalent compared with TPO-Abs (McLachlan & Rapoport, 1995; Saudra & Basil, 2004; Fink & Hintze, 2010). There were significant differences in the concentration of HLA-DR3 in all groups of patients in comparison with healthy subjects. Gebe et al., (2002) & Zaletel and Gaberscek (2011) reported that polymorphism sites within Class I and II of Histocompatibility complex play an important role in the occurrence of autoimmune diseases. Results revealed that a rise in incidence of Hypothyroidism in the first and second age groups, while the third age group showed an increase in incidence of disease in the Hyperthyroidism group. Peeters (2008) cleared that the change in production of thyroid hormones increases with age leading to disruptions of the thyroid gland in the elderly, also there was an increase in TPO and TG autoantibodies (Matthias & Scherbaum, 2006). The prevalence of hyperthyroidism in the elderly is increased, with frequencies ranging from 0.5-3% in population older than 60 years of age (Mariotti et al., 1995; Tunbridge et al., 1977; Hollowell et al., 2002; Diez, 2003).

References:

- [1]. Ahmed, K.H.; Taha, T.H. & Naji, H.T. (2004). Analysis of thyroid surgery for 100 patients in AL-Kadhimia teaching hospital. Iraqi-J. Med. Scie., 3(1):68-72.
- [2]. Ali, K.A.; Sharif, M.T.M. & Alwan, A.F. (2002). Determination of antithyroglobulin and antithyroperoxidase antibodies in patients with hyperthyroidism by application of ELISA technique. Iraqi-J. Comm. Med., 15(1):59-63.
- [3]. Ban, Y. (2012). Genetic Factors of Autoimmune Thyroid Diseases in Japanese. Hindawi Publishing Corporation. Article ID 236981, 9 pages.

- [4]. **Bishop , J.J., Name P.R., Popel A.S., Intaglietta M., Johnson P.C. (2000)** .Effects of erythrocytes aggregation on velocity profiles in venules. *Am. J. Physiol.*, 280, H1460.
- [5]. **Bjoro, J.; Kruger, O. & Midthjell, K.(2000)**.Prevalence of thyroid disease, thyroid dysfunction and thyroid peroxidase antibodies in large unselected population .*Eur. J. Endocrinol.*, 143(5):39-74.
- [6]. **Burmesters , G.R. & Pezzmto , A . (2003)**. *Color Atlas of Immunology* . thieme . Stuttgart , Germany .
- [7]. **Choksi , N. Y. ; Jahnke, G. D. ; Hilaire, C. St. & Shelby, M. (2003)** . Role of thyroid hormones in human and laboratory animal reproductive health. *Birth Defects Research (Part B)* ., 68:479–491 .
- [8]. **Lichiardopol, C. &Mota, M. (2009)**. The Thyroid and Autoimmunity. *Rom. J. Intern. Med.* , 47(3) : 207–215.
- [9]. **Devi, U.H. ; Vijay, R. ; Suchetha, K. N . & Sathyavathi R. A.(2012)** .
- [10]. Estimation of sialic acid, l-fucose and adenosine deaminase level in hypo and hyperthyroidism . *Asi . J. Pharma. Clin. Res.*, 5 (2):211-214 .
- [11]. **Diez , J.J. (2003)** . Hyperthyroidism in patients older than 55 years: an analysis of the etiology and management. *Gerontology* . 49: 316- 323.
- [12]. **Fairweather , D. (2007)**. *Autoimmune Disease : Mechanisms* . J. Hopkins University, Bloomberg School of Public Health, Baltimore, Maryland, USA.
- [13]. **Fink, H. & Hintze, G. (2010)** . Autoimmune Thyroiditis (Hashimoto's Thyroiditis): Current diagnostics and therapy. *Med. Klin. (Munich).*, 105(7): 485-493.
- [14]. **Gebe ,J.A.; Smanson ,E. & Kmok ,W.W. (2002)** . HLA class II peptide – binding and autoimmunity . *Tissue Antigens* ., 59:78-87
- [15]. **Harveg , R. A. & Champe , P. C. (2008)**. *Lippincott's Illustrated Reviews : Immunology* . Lippincott Williams and Wilkins , Awolters Klumer .
- [16]. Hasham, A, & Tomer, Y. (2012). Genetic and epigenetic mechanisms in thyroid autoimmunity. *Immunol Res.*, 54, 204-213.
- [17]. Hollowell, J.G. ; Staehling, N.W. ; Flanders, W.D. & et al. (2002). Serum TSH, T4, and thyroid antibodies in the United States population (1988 to1994): National Health and Nutrition Examination Survey (NHANES III). *J. Clin . Endocrinol . Metab* ., 87: 489-499.
- [18]. Jack, D.(2002). Thyroid hormone tutorial: thyroid pathology . *Endocrine Module (PYPP 5260)*, Thyroid Section.
- [19]. Janeway, C.A.; Travers, P.; Walport, M. & Shlomchik, M.J. (2005) *Immunobiology*. 6th edn . Garland Science. ISBN .
- [20]. Kenneth , M. ; Charles , A.J. ; Paul , T. & Mark , W. (2012) . *Janeway's Immunobiology* . 8th edn ., Garland Science . Taylor and Francis Group .
- [21]. Klein, I. & Levey, G.S.(2000) .The cardiovascular system in thyrotoxicosis. In: Braverman LE, Utiger RD, eds. *The thyroid*. 8th ed □ . Philadelphia: Lippincott-Raven ., 596-604.
- [22]. Kumar, D. C. ; Rameshwar , M. & Angoorbala, B . (2013) . Status of Circulating Markers of Thyroid Gland among the People of Indore city, Ind. Inter .Res .J. Med. Sci., 1(5): 15-18.
- [23]. Mansoor , R . ; Raza , S.S.; Kausar , W. ; Aslam , F ; Huda , S.T .(2011). Comparison of TSH, T4 and T3 levels in primary hypothyroidism in relation to gender and age in a tertiary care hospital . *Ann. Pak. Inst. Med. Sci.*, 7(4): 186-190.
- [24]. Mariotti, S. ; Franceschi ,C.; Cossarizza, A. & Pinchera ,A.(1995). The aging thyroid . *Endocrinol. Rev.* , 16: 686-715.
- [25]. Matthias S. & Scherbaum, A. W. (2006). Autoimmune thyroid disease. *Dtsch. Arztebl* . , 103(45): 3023–32.
- [26]. McLachlan, S.M. & Rapoport , B. (1995) . Genetic and epitopic analysis of thyroid peroxidase (TPO) autoantibodies: markers of the human thyroid autoimmune response. *Clin. Exp. Immunol.*,101(2): 200 – 206.
- [27]. Muhammad, O.K. (2009). Physiological changes in patients with hyperthyroidism. *Med .J. Baby.*, 6(3-4): 697 – 712.
- [28]. Pandiyan , B. (2011) . Mathematical modeling and dynamical analysis of the operation of the hypothalamus - pituitary -thyroid (HPT) axis in autoimmune hasimoto's thyroiditis . M.SC .thesis . University of Marquette .
- [29]. Peeters, R. P. (2008). Thyroid hormones and aging . *Hormones* ., 7(1):28-35..
- [30]. Saudra , M.M. & Basil , R . (2004).Why measure thyroglobulin autoantibodies rather than thyroid peroxidase autoantibodies ? *Thyroid* ., 14(7) : 510-520.
- [31]. Tunbridge ,W.M. ; Evered, D.C. ; Hall, R. & et al (1977) . The spectrum of thyroid disease in a community: the whickham survey. *Clin . Endocrinol . (Oxf)* ., 7: 481–493.
- [32]. Zaletel, K. & Gaberscek , S. (2011). Hashimoto's thyroiditis: from genes to the disease . *J. List. Curr. Genomics* ., 12(8) : 576–588.