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## **Evaluation of Thyroid Hormone Abnormalities and Thyroid Autoantibodies in Chronic Idiopathic Urticaria and Alopecia Areata Egyptian Patients**

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### **ABSTRACT**

Aim of the present study was to determine whether chronic urticaria or alopecia areata are statistically associated with thyroid dysfunction and/or thyroid autoimmunity in Egyptian population. The study comprised 35 CIU patients (mean age 28.1±10.2 years, 22 female versus 13 male) and 20 AA patients (mean age 27.2±12 years, 13 female and 7 male) as well as 30 control subjects (19 female and eleven male, mean age 26.3±12.2 years). All patients and control were subjected to thorough history taking, complete physical examination and routine laboratory tests. CIU and AA patients were otherwise clinically free and receive no medications. Free T3 (FT3), free T4 (FT4), Thyroid Stimulating Hormone (TSH), antithyroid peroxidase (TPA) and anti thyroglobulin (TGA) autoantibodies were evaluated for all patients and controls. On laboratory basis, clinical and subclinical thyroid disease was detected in 42.8% of CIU patients and 33.3% of AA patients versus subclinical hyperthyroidism detected in two control subjects. Mean serum levels of TSH, TPA and TGA were significantly higher in CIU patients or AA patients than control. This finding was preserved when comparing female CIU or AA patients with female control and male CIU and AA patients with male control. TPA was positive 14.2% of our CIU patients, TGA was found to be high in 20% of CIU patients. Moreover TGA was found to be high in 15% of AA patients, TPA tested +ve in 10% of our AA patients and equivocal in 15% of AA patients. No significant correlation between TPA or TGA and thyroid hormones in either CIU or AA patients was detected. Screenings for thyroid function and thyroid ultrasound are advisable in patients with CIU as well as AA patients for early detection of thyroid dysfunction. CIU and AA could help to discover a possible silent pathology of the thyroid gland in clinically euthyroid patients.

**Key words:** Thyroid autoantibodies, chronic idiopathic urticaria, alopecia areata, egyptian patients, thyroid hormone

### **INTRODUCTION**

Autoimmune thyroid disease has been associated with many other autoimmune disorders as insulin-dependent diabetes mellitus, rheumatoid arthritis, multiple sclerosis, systemic lupus erythematosus, chronic urticaria, alopecia areata and vitiligo (Cakir *et al.*, 2008).

Chronic urticaria is characterized by recurrent, transient itchy wheals occurring for more than 6 weeks. The term idiopathic (CIU) is often used when the cause remains elusive in spite of extensive investigations (Godse, 2004). Many studies suggested a link between thyroid autoimmunity and CIU as they found thyroid autoantibodies to thyroperoxidase (TPA) and thyroglobulin (TGA) elevated significantly more frequent in patients with chronic urticaria (Ryhal *et al.*, 2001). Koh *et al.* (2000) reported that clinical remission of CIU in euthyroid patients, with significantly elevated levels of TGA when treated with thyroxin but without change in the thyroid antibody level. Also, Milchert *et al.* (2007) reported successful treatment of CIU and mild arthritis associated with autoimmune thyroid disease with L-Thyroxine. However, other studies found no significant increased frequency of CIU in patients having thyroid disease (Verneuil *et al.*, 2004).

On the other hand, determination of the exact underlying etiology of Alopecia Areata (AA) is extremely problematic. Although many different pathogenic factors have been proposed, the contribution of the autoimmune process in the pathogenesis appears more convincing (Thomas and Kadyan, 2008). However, there is a lack of agreement on the overall prevalence of thyroid disease and thyroid function abnormalities in alopecia areata. The prevalence of thyroid disease with AA has been reported to vary widely from 0 to 28% (Sharma *et al.*, 1996; Puavilai *et al.*, 1994, 2007).

Therefore, aim of the present study was to determine whether chronic urticaria or alopecia areata are statistically associated with thyroid dysfunction and/or thyroid autoimmunity in Egyptian population.

## **MATERIALS AND METHODS**

This study was conducted on 35 patients with CIU (mean age 28.1±10.2 years, 22 female and 13 male), 20 patients with AA (mean age 27.2±12 years, 13 female and 7 male) and 30 healthy age and sex matched volunteers (19 female and eleven male, mean age 26.3±12.2 year) served as control. They were recruited from outpatient clinics of Dermatology Departments of Benha Teaching Hospital and Mansoura University Hospital. They come from 4 different Egyptian governorates nearly in equal proportions for patient groups and controls. CIU was diagnosed if urticarial lesions persisted more than 6 weeks and symptoms were present for most days of the week. CIU patients never had a history of drug, food, inhalant or insect bite allergy nor underlying infection anywhere. Subjects with family history of atopy and/or autoimmune disease as well as thyroiditis, Grave's disease or myxedema were excluded.

AA was diagnosed according to the definition of Olsen *et al.* (1999) and the pattern, main sites and extent of hair loss were recorded. The severity of the disease was defined as mild (< 3 patches of 3 cm or less), moderate (patch>3 cm in diameter or >3 patches) or severe with alopecia totalis or universalis (Kavak *et al.*, 2000).

Patients groups and controls with history of allergic disease (Bronchial asthma, asthmatic bronchitis, sinusitis, dermatologic disorders) or autoimmune disorders (ulcerative colitis, collagen vascular diseases, spondyloarthropathies and hemolytic anemia) were excluded.

### **All subjects underwent**

**Thorough history:** Taking previous scores for clinical diagnosis of hyper and hypothyroidism as a guide (Zulewski *et al.*, 1997; Wayne, 1965). They were inquired by unleading questions about: symptoms of hyperthyroidism (as anxiety, excessive sweating, preference to cold, dyspnoea, palpitation, tiredness, weight loss, appetite change, bowel habit and menstrual changes; eye

symptoms including star look, eye protrusion, redness, soreness, watering, peri-orbital puffiness, or double vision and symptoms of hypothyroidism including slow movements, fatigue, cold intolerance, diminished sweating, hoarseness of voice, coarse skin, weight gain, hearing changes, cold skin, constipation. Subjects with symptoms of hyper or hypothyroidism, past-history of thyroid disease or thyroid medications or medication affecting thyroid gland or thyroid hormone level were excluded.

**Complete physical examination:** With stress on eye signs (exophthalmos, lid lag, external ocular movement, conjunctivitis, sensations), ankle jerk, neurological examination and thyroid gland examination for size, consistency, pulsation and auscultation. Thyroid gland examination was normal for healthy and control.

- Routine laboratory tests were normal for patients and controls (serum creatinine, liver function tests, CBC and ESR, plasma glucose level)
- CIU and AA patients were otherwise clinically free and receive no medications as well as controls
- **For laboratory evaluation:** Ten milliliter venous blood samples were collected in the morning after 8 h fasting and divided in two 5 mL samples for each patient. Sera were stored at  $-70^{\circ}\text{C}$  till the time of the analysis. All hormone and antibody levels were estimated by 2 experienced hand twice for each patient for average value to be calculated
- **Quantitative evaluation** of serum levels of Free Tri-iodothyronine ( $\text{FT}_3$ ), Free Thyroxine ( $\text{FT}_4$ ), Thyroid Stimulating Hormone (TSH), Anti-Thyroid Peroxidase (TPA) and anti-thyroglobulin (TGA) autoantibodies was done. Free T3 and free T4 were measured in the collected samples by the use of Dima kits provided by Dima Gesellschaft fur Diagnostika. The principle of the assay was competitive enzyme immunoassay (Young *et al.*, 1975). It was a solid phase enzyme immunoassay in which mixing immobilized antibody, enzyme-antigen conjugate and a serum containing the native free antigen results in a competition reaction between the native free antigen and the enzyme-antigen conjugate for a limited number of binding sites. Then the antibody-bound fraction was separated from unbound antigen by aspiration. The enzyme activity in the antibody-bound fraction was inversely proportional to the native free antigen concentration which is measured from the curve done by the use of different serum references, reference range for free T3 was  $1.4\text{-}4.2\text{ pg mL}^{-1}$ , for free T4 was  $0.8\text{-}2\text{ ng dL}^{-1}$

TSH was measured by the use of DRG kit provided by DRG International, Inc. USA. The principle of the assay depends on ELISA technique using an immobilization antigen, circulating antibody and enzyme-linked specific antibody (Engall, 1980; Van Vunakis, 1980). In this procedure, the immobilization took place during the assay at the surface of the micro plate well through the interaction of 8 strap taviden coated on the well and exogenously added biotinylated antigen. Reference range for TSH was  $0.45\text{-}5\text{ IU mL}^{-1}$ .

TPA was measured by the use of Zeus kit provided from Zeus scientific, Int. USA. The principle of the assay depended on (TPA) ELISA test system, designed to detect IgG class antibodies to TPA in human serum wells of plastic micro well strips, sensitized by passive absorption with TPA antigen (Tung *et al.*, 1974). TPA considered -ve if  $<25\text{ IU mL}^{-1}$ , Equivocal if between  $25\text{-}30\text{ IU mL}^{-1}$  and +ve  $>30\text{ IU mL}^{-1}$ .

The quantitative determination of TGA by microplate enzyme immunoassay, using kits from MONBIND, Inc. (USA) (Volep, 1994). TGA reference for normal was  $74.3 \pm 25.2$  IU mL<sup>-1</sup> as a mean (range from 49.1 to 99.5 IU mL<sup>-1</sup>).

CIU patients were classified into 2 subgroups. Subgroup with disease duration < 2 years (n = 13) and the other with disease duration >2 years (n = 22). They further subdivided into 2 subgroups according to TSH level. Subgroup with increased TSH level (n = 14) and the other with normal or low TSH level (n = 21).

AA patients were categorized into 2 subgroups: subgroup included 13 patients with mild AA and subgroup included 7 patients with moderate AA, other two subgroups according to TSH levels.

Subclinical thyroid disease is diagnosed when T3 and T4 levels are normal but serum TSH below reference range (subclinical hyperthyroidism) or above reference range (subclinical hypothyroidism) (Surkas *et al.*, 2004).

**Statistical analysis:** The data were presented in the form of number and percentage. Computer analysis included difference between groups using the student t-test and Spearman's correlation test. All these tests were considered significant if p-value < 0.05.

## RESULTS

Our studied CIU sample was found on laboratory basis to include 11 patients with subclinical hypothyroidism (31%), 3 patients with hypothyroidism (8.5%) and one patient with hyperthyroidism (2.85%). TGA was high in 7 patients (20%) (One hyperthyroid, 2 hypothyroid, 2 subclinical hypothyroidism and 2 euthyroid patients). TPA was +ve in 5 patients (14.2%); (2 hypothyroid, 1 subclinical hypothyroidism and 2 euthyroid patients) and equivocal in 4 patients (11.42%) (3 subclinical hypothyroidism and one euthyroid patient (Table 1). It is to be reported that two control subjects could be classified as subclinical hyperthyroidism and another one had TPA equivocal level (data not showed). Mean serum level of TSH, TPA and TGA were significantly higher in CIU patients than control (Table 1, 2). This relation was preserved when we compared female and male CIU with their counter controls (Fig. 1-3). CIU patients with disease duration >2 years showed significantly higher TPA levels (Table 3). Present studied patients with AA on laboratory basis were found to include one patient with subclinical hyperthyroidism (5%), 5 patients with subclinical hypothyroidism (25%). TGA was found to be high in 3 AA patients (15%), (two euthyroid and one with subclinical hypothyroidism).

Table 1: Distribution of thyroid hormones and autoantibody levels in the 2 patient groups

	CIU (N = 35)						AA (n = 20)					
	High		Normal		Low		High		Normal		Low	
	N.	%	N.	%	N.	%	N.	%	N.	%	N.	%
Free T3	5	14.2	21	60.00	9	25.7	1	5	14	70	5	25
Free T4	2	5.7	27	77.19	6	17.1	-	-	16	80	4	20
TSH	14	40.0	20	57.10	1	2.85	5	25	14	70	1	5
TGA	7	20.0	23	65.70	5	14.2	3	15	11	55	6	30
TPA	+ve		Equivocal		-ve		+ve		Equivocal		-ve	
	5	14.2	4	11.42	26	74.2	2	10	3	15	15	75

Table 2: Studied clinical and laboratory parameters in chronic urticaria and alopecia areata patients versus controls

Parameters	Studied groups				
	Chronic urticaria (N =35)	Alopecia areata (N = 20)	Controls (N = 30)	t <sub>1</sub> CIU patients vs. control	t <sub>2</sub> alopecia areata patients vs. control
	Mean±SD	Mean±SD	Mean±SD		
Age in years	28.10±10.2	27.2±12	26.30±12.2	0.625 (NS)	0.026 (NS)
Duration in years	5.00±4.1	2.0±1.3	-	-	-
Free T3 (pg mL <sup>-1</sup> )	1.40±1.9	2.2±1.3	1.97±0.4	1.667 (NS)	0.833 (NS)
Free T4 (ng dL <sup>-1</sup> )	0.95±0.4	1.1±0.4	0.90±0.1	0.543 (NS)	1.98 (NS)
TSH (uIU mL <sup>-1</sup> )	4.20±4.3	3.5±2.6	1.40±0.5	3.784***	3.5***
TPA (IU mL <sup>-1</sup> )	19.30±5.3	20.6±5.5	12.40±1.5	6.667***	5.923***
TGA (IU mL <sup>-1</sup> )	221.40±320.1	132.1±166.1	69.10±8.9	2.63*	1.425 (NS)

N: No., NS: Non significant, \*p<0.05, \*\*p<0.01, \*\*\*p<0.001

Table 3: Comparison of the studied clinical and laboratory parameters in different subgroups of patients with chronic urticaria

Parameters	Studied groups						
	CIU<2 years		CIU>2 years		Urticaria normal or low TSH		t <sub>1</sub> group CIU + TSH vs. normal or low TSH
	N = 13 Mean±SD	N = 22 Mean±SD	Urticaria + TSH N = 14 Mean±SD	Urticaria normal or low TSH N = 21 Mean±SD	t <sub>2</sub> CIU <2 years vs. CIU>2 years		
Age in years	32.0±11	25.8±9.2	22.3±5.7	33.10±9.5	1.72 (NS)	4.154**	
Duration in years	1.1±0.7	7.3±3.4	5.0±2.9	5.10±4.3	7.75***	0.083 (NS)	
Free T3 (pg mL <sup>-1</sup> )	0.9±1.3	1.7±2.2	1.9±2.2	1.20±1.8	1.35(NS)	0.877 (NS)	
Free T4 (ng d <sup>-1</sup> )	0.9±0.4	1.0±0.4	0.9±0.4	1.00±0.4	1.00 (NS)	0.571 (NS)	
TSH (uIU m <sup>-1</sup> )	4.3±6.4	4.2±2.7	8.1±5.0	2.03±1.3	0.05 (NS)	8.912***	
TPA (IU m <sup>-1</sup> )	15.8±4.7	21.5±4.7	19.9±6.1	18.70±4.8	3.38**	0.7 (NS)	
TGA (IU m <sup>-1</sup> )	171.4±79	247.8±400.1	151.3±104.6	265.70±401	0.878(NS)	1.2625 (NS)	

N: No., NS: Non significant, \*p<0.05, \*\*p<0.01, \*\*\*p<0.001

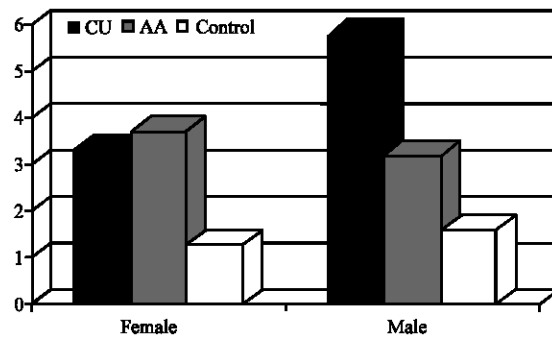


Fig. 1: TSH level in female and male patients groups compared with male and female control group

TPA was positive in 2 AA patients, (one euthyroid and the other with subclinical hypothyroidism) and equivocal in 3 euthyroid patients (Table 1). Serum levels of TSH and TPA were significantly higher in AA patients than control (Table 2); this relation was preserved while

Table 4: Comparison of the Studied clinical and laboratory parameters in subgroups of patients with alopecia areata

Parameters	Studied groups					
	Mild alopecia areata N =13 Mean±SD	Moderate alopecia areata N = 7 Mean±SD	Alopecia areata ↑ TSH N = 5 Mean±SD	Alopecia areata Normal (14) or low (1) TSH N = 15 Mean±SD	Mild alopecia areata vs. Moderate alopecia areata group t1	Alopecia areata with ↑ TSH vs. alopecia areata with normal or low TSH t2
Age in years	19.40±7.7	38.1±9.2	24.6±7.2	26.1±14.1	4.561***	0.3
Duration in years	1.10±0.6	3.3±1.0	1.5±0.8	2.0±1.4	5.366***	1.0
Free T3 (pg m <sup>-1</sup> )	1.90±1.3	2.8±1.0	1.1±0.8	2.6±1.3	1.73 (NS)	3.0**
Free T4 (ng d <sup>-1</sup> )	1.04±0.4	1.2±0.5	0.7±0.2	1.3±0.4	0.727 (NS)	4.4285***
TSH (uIU m <sup>-1</sup> )	4.60±2.3	2.3±2.5	7.3±0.6	2.7±1.4	2.018 (NS)	9.8***
TPA (IU m <sup>-1</sup> )	21.20±5.6	19.1±5.4	20.9±5.9	20.1±5.7	0.808 (NS)	0.3
TGA (IU mL <sup>-1</sup> )	118.00±128.8	152.4±230	77.3±21.3	151.3±195.1	0.429 (NS)	1.45

N: No., NS: Non significant, \*p<0.05, \*\*p<0.01, \*\*\*p<0.001

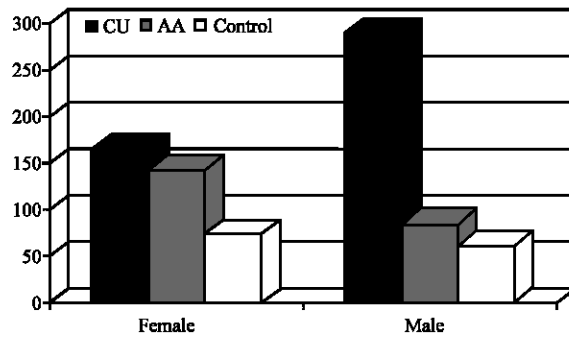


Fig. 2: TGA level in female and male patients groups compared with male and female control group

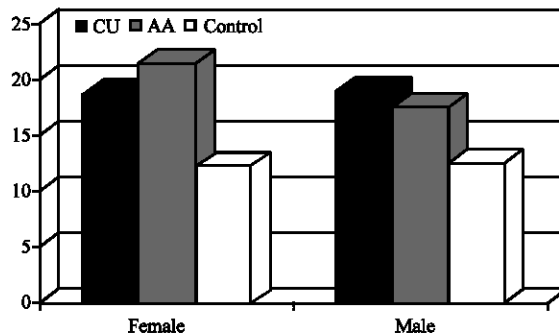


Fig. 3: TPA level in female and male patients groups compared with male and female control group

comparing female and male AA patients with their counter controls (Fig. 1, 3). NO significant findings were found in subgroups of AA regarding TPA and TGA levels (Table 4). No significant correlation was found between TPA or TGA and thyroid hormone level in CIU and AA patients (Table 5).

Table 5: Correlations of antithyroid Antibodies to the studied clinical and laboratory parameters in chronic urticaria patients and alopecia areata patients

Parameters	Studied groups			
	TPA in chronic urticaria (N = 35)	TPA in alopecia areata (N = 20)	TGA in chronic urticaria (N = 35)	TGA in alopecia areata (N = 20)
Age in years	-0.072 (NS)	-0.231(NS)	-0.05 (NS)	-0.189 (NS)
Duration in years	0.324 (NS)	-0.411 (NS)	0.163 (NS)	0.137 (NS)
Free T3 (pg mL <sup>-1</sup> )	0.15 (NS)	-0.364 (NS)	-0.002 (NS)	0.13 (NS)
Free T4 (ng dL <sup>-1</sup> )	0.0235 (NS)	0.363 (NS)	0.9±0.1 (NS)	0.195 (NS)
TSH (uIU mL <sup>-1</sup> )	0.0235 (NS)	0.099 (NS)	0.05 (NS)	-0.097 (NS)

N: No., NS: Non significant, \*p<0.05, \*\*p<0.01, \*\*\*p<0.001

## DISCUSSION

CIU is a cause of serious personal, social and occupational disability which virals that of coronary artery disease (DeMarco, 2008). It is very rarely found to be an atopic phenomenon.

The association between CIU and thyroid autoimmunity has been a subject of debate. Some authors found a higher frequency of thyroid autoantibodies in CIU, while no significant frequency of CIU was found in patients with/without thyroid antibodies in thyroid diseases (Verneuil *et al.*, 2004).

While many studies investigated the relation between autoimmune thyroid diseases and autoimmune urticaria, fewer studies dealt with clinically euthyroid patients with CIU moreover, their results varied widely in different populations. Also, many studies suggested a link between thyroid microsomal autoantibodies and CIU but they are less sensitive and less specific than anti-thyroperoxidase autoantibodies (Verneuil *et al.*, 2004). This study is designed to declare whether CIU and AA are statically associated with thyroid dysfunction and or thyroid autoimmunity in Egyptians.

In the present study, TSH level was increased in 40% of CIU patients (14 patients), FT4 levels were mildly decreased in 17.1% of CIU patients (6 patients), FT3 levels were decreased in 25.7% of CIU patients (9 patients). Present studied CIU sample was found on laboratory bases to be comprised of 11 patients with subclinical hypothyroidism (31%), 3 patients with hypothyroidism (8.5%) and one patient with hyperthyroidism (2.85%). TGA was high in 7 patients (20%, one hyperthyroid, 2 hypothyroid, 2 subclinical hypothyroidism and 2 euthyroid patients). TPA was +ve in 5 patients (14.2%, 2 hypothyroid, 1 subclinical hypothyroidism and 2 euthyroid patients) and equivocal in 4 patients (11.42%, 3 subclinical hypothyroidism and one euthyroid patient) (Table 1). It is to be reported that 2 control subjects could be classified as subclinical hyperthyroidism.

These results were higher than the results reported by Turktas *et al.* (1997) and Kandeel *et al.* (2001) they reported that the incidence of abnormal thyroid function, either increased or decreased FT4 or increased or decreased TSH or both was 12-19%. Also, O'Donnell *et al.* (2005) reported that TSH level outside the normal range was found in one skin test-negative patient out of 92 skin test -ve studied group and stressed that this percent is comparable to the expected prevalence in the community.

Present results may reflect higher incidence of subclinical hypothyroidism in our sample and high lights the necessity of thyroid ultrasound as a part of routine evaluation of the thyroid gland and/or skin test for definite diagnosis of CIU. However, the higher incidence of thyroid



autoimmunity in this Egyptian sample of CIU patients could not be simply and accurately explained as broad non-specific autoimmunity as HLA typing was not evaluated. Also, hepatitis C-virus infection with its well known higher incidence in Egypt and autoimmune manifestations was not excluded.

In this study TPA was positive in 14.2% of our CIU patients (3 females and 2 males) and equivocal in 11.42% patients (2 females and 2 males). These results were comparable to results of Zauli *et al.* (2001), they found that their studied CIU group were positive for at least one type of thyroid antibody in 23% of patients. However, TPA level was found to be high in two control subject in our study.

Also, Ryhal *et al.* (2001) reported that in their study of CIU patients, non of whom had overt thyroid disease, TPA was found to be positive in 20% of their patients compared to 0% in their control group.

In this study, TGA was found to be high in 20% of CIU patients (7 patients, 3 male and 4 females). Similar results has been reported by Kulthanan *et al.* (2007), who found TGA positive in 16% of CIU patients in Thailand. However, Turtkas *et al.* (1997) reported that 11.7% of their patients of CIU and/or angiodema were found to have thyroglobulin antibodies and 9.57% were found to have thyroid microsomal antibodies compared with both antibodies being found in 3.7% of the control group. On the other hand, our results are much far from the results of Sabroe and Greaves (1997), they reported that the incidence of thyroid autoimmunity in CIU is probably no greater than that of general population, they acknowledge that there is clustering of thyroid microsomal antibodies in patients with positive autologous serum skin test.

Other authors reported that the frequency of thyroid autoantibodies was higher in patients with CIU than in healthy controls (26.7% versus 3.3%), however all of their studied patients with thyroid autoantibodies had thyroid hormone concentrations within normal limits (Verneuil *et al.*, 2004).

Also, Aamir *et al.* (2008) reported elevated titres of TGA and antimicrosomal antibodies in female patients with CIU in a higher percent (30 and 43.3%, respectively).

More recently, Gangemia *et al.* (2009), in Italy found that 32.6% of their CIU investigated group tested positive for at least one antithyroid antibody (TGA or TPA), they also reported that their findings were higher than previous findings in northern Italy.

Some authors also reported that their patient was clinically euthyroid at the start of their CIU but became hyperthyroid clinically and laboratory within 3 month. They also found that their CIU was improved with normalization of thyroid function (Bansal and Hayman, 2009). Other authors also reported that treatment with thyroxine has brought about clinical remission in an euthyroid patient with CIU with evidence of significantly elevated levels of thyroglobulin and microsomal antibodies but no change in the thyroid antibody level could be demonstrated (Koh *et al.*, 2000). However, others reported that there are no compelling argument to decide whether or not thyroid autoimmunity plays a significant role in the pathogenesis of chronic urticaria as patients with chronic urticaria and biochemical evidence thyroid autoimmunity may have active thyroid disease or may be clinically euthyroid (Dreskin and Andrew, 2005).

The mechanism by which thyroid autoimmunity is associated with CIU is poorly understood. A cross-linking of IgE receptors of mast cells by antithyroid antibodies may presumably be a cause of histamine release. The presence of anti-thyroperoxidase antibody IgE in a patient with chronic urticaria suggested that these IgE autoantibodies might play a pathogenic role in urticarial

symptoms, sensitizing mast cells and inducing its degranulation. Anti thyroperoxidase IgE could cross-react with peroxidase contained in vegetables. So, the ingestion of some peroxidase-containing vegetables could trigger urticaria (Bar-Sela *et al.*, 1999).

There are no data to suggest that any of the antithyroid antibodies is pathogenic in terms of CIU and most likely these are associated parallel autoimmune event (Rottem, 2003). Antithyroid antibodies are not supposed to be pathogenic factors responsible for and generated from the recruitment of inflammatory cells (i.e., proinflammatory cytokines, histamine-releasing factors and autoantibodies) (Rumbyrt *et al.*, 1995).

In this study, the lack of significant correlation between TPA and TGA with thyroid hormones not supports the idea of causal relationship in those patients with apparently normal thyroid. Thyroxine treatment lowers the level of thyroid stimulating hormone that may result in control of release something from inflamed thyroid gland that cause urticaria may be considered possible explanation. Some authors supposed improvement of CIU with thyroid hyperactivity treatment may be due to reduction in body's metabolism and the sensation of over heating experienced when thyroid hyperactivity is reduced as many patients with CIU and no underlying thyroid dysfunction also experience worsening of their condition when they are hot and sweaty (Bansal and Hayman, 2009).

AA is a common cause of non cicatricial alopecia that occurs as patchy, confluent or diffuse pattern. It may occur as a single, self-limiting episode or may recur at varying intervals over many years. Strong direct and indirect evidence supports an autoimmune etiology for AA. The origin of disease is not fully understood; however, there are indications for a T-cell mediated autoimmune process directed against an unknown autoantigen of the hair follicle. T lymphocytes that have been shown to be oligoclonal and autoreactive are predominantly present in the peribulbous inflammatory infiltrate (Hordinsky and Ericson, 2004).

Histologic studies have showed increased activated CD3+ HLA-DR+ in peripheral blood of patients with AA with their infiltration seen in the epithelial cells of hair follicles and epidermal keratinocytes (Kurtev and Iliev, 2005). Also significant differences have been identified in the profile of AA among different societies (Nanda *et al.*, 2002).

This autoimmune etiology has been also proposed on the basis of its association with various autoimmune disease, the presence of auto-antibodies and various underlying immunologic abnormalities in the affected sites of these patients (Thomas and Kadyan, 2008).

In this study, FT3 levels were high in 5% of AA patient (1 female patient) and low in 25% of patients (5 patients, 3 females and 2 males). Free T4 was found to be low in 20% of patients (4 patients, 2 males and 2 females) TSH was high in 25% of patients (5 patients, 3 females and 2 males) and low in 5% of patients (1 female patient). Accordingly, our AA patients on laboratory bases comprised one patient with subclinical hyperthyroidism (5%) and 5 patients with subclinical hypothyroidism (25%). TGA was found to be high in 15% of AA patients, TPA tested +ve in 10% of our AA patients and equivocal in 15% of AA patients.

Thomas and Kadyan (2008) reported that evident hypothyroidism was found in 14.1% of their studied patients.

Sharma *et al.* (1999) found abnormal thyroid hormone levels in 11.3% of their studied patients and elevated autoantibodies (TGA and TPA) in 8% of their studied AA patients.

Korkij *et al.* (2006) found TGA and TPA in 28% of their studied patients.

Also, Kasumagic-Halilovic (2008) found abnormal thyroid function in 11.4% of their investigated AA patients as well as positive TGA and TPA in 25.7% of the same group.

Puavilai *et al.* (1994) estimated lower incidence of thyroid disease in AA patients (7.2%) which was not statistically different from controls.

Seyrafi *et al.* (2005), found thyroid function abnormalities in 8.9% of their patients.

Also, autoantibodies were positive in 51% of their patients (TGA), however, they could not found possible explanation for such higher incidence rather than racial and genetic factors.

Also, some authors reported increased basal TSH levels in 13.3% increased TGA in 39.5% and increased antimicrosomal antibodies in 33.3% in their studied group of children and adolescents of both sex with AA, however, in their study, thyroid ultrasound examination was suggestive of autoimmune thyroiditis in 34.2% and typical of autoimmune thyroiditis in 13.2% of their patients (Kurtev and Iliev, 2005).

Similar results has been reported by Grandolfo *et al.* (2008) they also found that autoantibodies against thyroperoxidase and thyroglobulin more frequently in patients with AA.

On the other side, other authors reported no significant difference in the incidence of thyroglobulin and thyroid complement fixing antibodies in patients with alopecia areata (Cunliffe *et al.*, 1969).

We could support the idea of existence of significant association between thyroid disorders and alopecia areata, we find the assumption of formation of organ-specific autoantibodies that may play a pathogenic role in both disorders is good possible explanation (Thomas and Kadyan, 2008).

The effect of hypothyroidism on hair includes changes in hair texture as well as alopecia of the scalp. This could be contributed to delay or failure of resumption of anagen hair due to decreased metabolic rate which lead to loss of hair without replacement as well as increased telogen hair counts (club hairs) before gradual shedding (Thomas and Kadyan, 2008). However, not all patients with hypothyroidism have AA as the effect of thyroid hormone on hair growth is variable and conditioned by local factors and other systemic influences.

## CONCLUSION

Screening for thyroid function and thyroid ultrasound are advisable in all patients with CIU and AA for the early identification of patients requiring either treatment of underlying thyroid dysfunction or follow up.

Patients with chronic urticaria and biochemical evidence of thyroid dysfunction may be clinically euthyroid and they required programmed thyroid follow up.

AA could be related to other autoimmune diseases and it could help to reveal a silent pathology of thyroid gland.

## Limitations:

- Small number of subjects included in the study due to wide spectrum of exclusion criteria and high cost for accurate doubled laboratory measurements

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