


" Clinical Profile of Patients with Hyperthyroidism in Zagazig University Hospitals "

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Abstract

Background

Hyperthyroidism is a condition that occurs due to over production of thyroid hormones by the thyroid gland . It can be categorized according to thyroid hormone levels into overt and subclinical hyperthyroidism. Also could be classified into, normal (or high) and low thyroid radioactive iodine uptake according to radioiodine uptake. Diagnosis and identification of each category of hyperthyroidism is based on assay of thyroid hormones plus thyroid gland scintigraphy. So, the aim of this study was to evaluate the difference in clinical and biochemical profile between hyperthyroid patients and its relation to thyroid scan imaging, for better management and follow up of hyperthyroid patients. Also to avoid prescribing antithyroid medications to patients with thyroiditis, this could lead to hypothyroidism or other side-effects

Materials and methods: This is a prospective cohort study for patients with hyperthyroidism. Patients have been enrolled from Endocrinology Outpatient Clinic at Zagazig University Hospitals in the period from December 2018 to October 2020.

Results: patients were divided into two major groups, overt hyperthyroidism (group 1) and subclinical hyperthyroidism (group 2). All patients of group (1) had abnormal thyroid gland examination but, only 50 % of group (2) patients had showed abnormal gland examination ($p < 0.001$). 83.3% of patients of group (1) had high thyroid uptake and 62.5 % of patients of group (2) had high thyroid uptake ($p = 0.108$). As regard thyroid hormones, there was highly statistical significance between the two groups as regard F. T4($P = < 0.001$) and F.T3 ($p = < 0.001$), but no difference in TSH($p = 0.223$).

Conclusion: The thyroid scan had cross linkage with abnormal thyroid clinical and biochemical data, helping in differentiating the causes of overt hyperthyroid and subclinical hyperthyroid dysfunction.

Keywords: hyperthyroidism; categories; scan.

Introduction:

Hyperthyroidism is a medical disorder that occurs due to release of abnormal higher levels of thyroid hormones by the thyroid gland to be differentiated from thyrotoxicosis, which is defined as the condition that occurs due to overproduction of thyroid hormone due to any cause and so includes hyperthyroidism ^[1]. Subclinical hyperthyroidism is characterized by depressed levels of serum thyroid stimulating hormone (TSH) with free triiodothyronine (FT3) and free thyroxin (FT4) levels within laboratory reference ranges ^[1]. According to radioiodine uptake two categories can be identified, normal or high thyroid radioactive iodine uptake (thyrotoxicosis with hyperthyroidism or true hyperthyroidism) and low thyroid radioactive iodine uptake (Thyrotoxicosis without hyperthyroidism is caused by extra thyroidal source of thyroid hormone or by a release of preformed thyroid hormones into the circulation) ^[2] . The above normal levels of thyroid hormones are harmful to many different organ systems. Most of the patients presented with palpitations, fatigue, tremor, anxiety, disturbed sleep, weight loss, heat intolerance, sweating, and polydipsia. Frequent physical findings are tachycardia, tremor of the extremities, and weight loss ^[3]. Diagnosis of thyrotoxicosis is mainly based on assay of thyroid hormone levels, first serum TSH should be estimated because it has the highest sensitivity and specificity in the diagnosis of thyroid disorders. If low, serums free T4 or free T4 index, and free or total T3 concentrations should be assessed to distinguish between subclinical hyperthyroidism and overt hyperthyroidism ^[4]. Thyroid scans and uptakes had important role in discrimination of type of thyrotoxicosis, as well as diffuse and localized over activity ^[5].

Patient and methods:

This prospective cohort study was planned to evaluate 48 patients with hyperthyroidism. They were categorized into two groups ,group (1) 24 patients

with overt hyperthyroidism , and group (2) 24 patients with subclinical hyperthyroidism . Group (1) overt hyperthyroid patients: recently diagnosed or already on antithyroid drugs treatment, whom had supra normal levels of (T4, T3) and low TSH.

Group (2) subclinical hyperthyroid group: patients whom originally subclinical hyperthyroidism or developed subclinical hyperthyroidism during course of treatment of hyperthyroidism, with normal levels of (T4, T3) and low TSH. All were from 18 to 65 years old, both sexes included in the study excluding pregnant and lactating females. All of them must have low suppressed TSH level. They were enrolled from the Outpatient Clinic at Zagazig University Hospitals in the period from December 2018 to October 2020. Clinical and laboratory data were obtained such as age, gender, neck examination, eye examination and routine laboratory investigations .Plus, thyroid function tests and thyroid scan examination. All subjects participated in the study provided written informed consent. The study was approved by the research ethical committee of Zagazig University's Faculty of Medicine.

Testing for TSH, free T3 and free T4: Blood sample collection: 5 ml of peripheral fasting venous blood were taken from each subject under complete aseptic conditions, Each sample left for 30 minutes for spontaneous clotting then centrifuged at 3000 rpm for 5 minutes to obtain serum samples and kept frozen until the time of assay of thyroid function (TSH, FT3 and FT4).

TSH: Human thyroid stimulating hormone ELISA kit, Inteco Diagnostics UK Ltd, 62 Beechwood Road, E8 3DY England. This test is based on the principle of a solid phase enzyme-linked immunosorbent assay. The TSH present in the sample originates a coloured complex. The intensity of the colour formed is directly proportional to the TSH concentration in the sample.

FT3: Human Free Triiodothyronine (F-T3) ELISA kit, Catalog No. E1004. AUTOBIO Diagnostics Co., LTD, Zhengzhou, China. The free T3 present in the

sample originates a coloured complex. The color intensity is inversely related to the concentration of free T3 in the test sample.

FT4: Human Free thyroxine (F-T4) ELISA kit, Catalog No. E1005. AUTOBIO Diagnostics Co., LTD, Zhengzhou, China. The free T4 present in the sample originates a coloured complex. The color intensity is inversely related to the concentration of free T4 in the test sample.

The research was conducted out in conformity with the World Medical Association's Code of Ethics (Declaration of Helsinki) for human studies..

Statistical analysis:

Data analysis was performed using the software SPSS (Statistical Package for the Social Sciences) version 20 (IBM corp. Released 2011. IBM SPSS statistics for windows, Version 20.0. Armonk, NY: IBM Corp.). Quantitative variables were described using their means and standard deviations. Categorical variables were described using their absolute frequencies. To compare means of two groups, independent sample t test (used with normally distributed data) was used and to compare medians of two groups, Mann whitnet test (used with not normally distributed data) was used. Focusing on the differences in the levels of (TSH, FT4 and FT3) between the both groups of study. Also noticed the difference between clinical signs in both groups .P value that was ≤ 0.05 , considered statistically significant.

Result:

Forty eight patients were included in the study; they were classified into two groups, 24 patients with overt hyperthyroidism (group 1) and another 24 patients with subclinical hyperthyroidism (group 2). Table (1) illustrates the difference between the two groups as regard age, sex and BMI. Female predominance was significantly evident in group (1) patients than group (2) ($p=0.008$). Age also was

significantly different between two groups, in the group (1) median age was 35 and the group (2) median age was 49 (p=0.001). On the contrary there was no Statistical significance (p=0.137) for BMI between two groups. Median BMI for group (1) was 29.9 and for group (2) median was 28.6.

Table (1) : Clinico-demographic data in overt hyperthyroid group(1) and subclinical hyperthyroid group (2):

		Group				Test	P
		Overt(group 1) Hyperthyroidism		Subclinical (group 2) Hyperthyroidism			
		N	%	N	%		
Sex	F	22	91.7%	14	58.3%	7.1	*0.008
	M	2	8.3%	10	41.7%		
Age (years)	Mean ±SD	37±12		50±10		-3.8	**<0.001
	Median	35 (22-60)		49 (36-70)			
BMI Kg/m ²	Mean ±SD	29.8±2.5		28.6±2.4		-1.5	0.137
	Median	29.9 (25.5-33.6)		28.6 (24.8-32.4)			

All variables were compared using Independent T test except (*) Chi-square X² test, (F) female, (M) male and (BMI) body mass index. ;[Continuous data are presented as median (range) or n (%)].

As shown in table (2) all patients of group (1) had abnormal thyroid examination 54.2% of patients of group (1) had diffusely enlarged thyroid gland and the remaining 45.8 % of them had nodular enlargement . On the contrary , 50 % of group (2) patients had showed no abnormalities ,41.7% with nodular enlargement and only 8.3 % of them showed diffusely enlarged thyroid gland with highly significant difference between two groups (p= <0.001). As regard eye examination 50 % of group (1) patients had eye abnormality on examination (33.3 % starring look and 16.7 % with exophthalmos) and the other 50% showed no abnormality while 75 % of group (2) patients showed no abnormality and only 25 %

of these patients had eye abnormality (16.7 % of them had starring look and 8, 3% showed exophthalmos) .But, we noticed there was no significant difference between two groups in eye abnormalities (p= 0.074) .

Table (2): Clinical findings in overt hyperthyroid group(1) and subclinical hyperthyroid group (2): as regard neck examination for thyroid gland abnormality and presence or absence of eye abnormality (exophthalmos or starring look):

		Group				X ² Test	P
		Overt Hyperthyroidism (group 1)		Subclinical Hyperthyroidism (group 2)			
		N	%	N	%		
Neck Exam	No abnormality	0	0.0%	12	50.0%	20.1	* <0.001
	Diffuse Enlarg.	13	54.2%		2		
	Nodular Enlarg.	11	45.8%		10		
Eye Exam.	Exophthalmos	4	16.7%	2	8.3%	3.2	0.202
	Starring	8	33.3%	4	16.7%		
	N	12	50.0%	18	75.0%		

Table (3) showing 83.3% of patients of group (1) had high thyroid uptake and only 16.6% with normal uptake. On the other hand 62.5 % of patients of group (2) had showed high thyroid uptake and 37.5 % with normal uptake by thyroid gland . But , there was no significant difference between the two groups (p=0.108) .

Table (3) : Thyroid Scan findings in overt hyperthyroid group(1) and subclinical hyperthyroid group (2):

		Group				X ² Test	P
		Overt Hyperthyroidism (group 1)		Subclinical Hyperthyroidism (group 2)			
		N	%	N	%		
Thyroid Scan	High Uptake	20	83.3%	15	62.5%	2.6	0.108
	Normal uptake	4	16.6 %	9	37.5 %		

Table (4) showed that in group (1)patients the median TSH level was 0.02 ,median for F.T4 level was 26.09 and F.T3 median level 8.32 . In group(2) patients TSH median was 0.04 ,F.T4 median was 21.0 and F.T3 median was 5.75 .We noticed that there was a highly statistical significant variation between the two groups as regard F. T4(P = <0.001) and also F .T3 (p = <0.001), but no significant difference in TSH(p =0.223) .

Table (4) : Thyroid profile in both groups (markers for thyroid function : (TSHm – F. T4- F. T3) :

	Group				Total		MW-test	P
	Overt Hyperthyroidism (Group 1)		Subclinical Hyperthyroidism (Group 2)		Median	Range		
	Median	Range	Median	Range				
TSH μ IU/mL.	0.02	0.01-0.08	0.04	0.01-0.12	0.03	0.01-0.12	-1.2	0.223
F.T 4 (pmol/l	26.09	22.00-35.81	21.00	18.00-23.70	23.00	18.00-35.81	-5.4	**0.001
F.T3 (pmol/l	8.32	6.90-12.00	5.75	3.60-7.00	7.00	3.60-12.00	-5.8	**<0.001

TSH (thyroid stimulating hormone) , F.T4 (free throid hormone T4) , F .T3 (free thyroid *

** $p \leq 0.001$ is statistically highly significant

This table (5) shows that most of the cases of overt hyperthyroidism group (1) were Grave's disease (50.0%) while 33.3 % diagnosed with multinodular goiter and only 16.7% had toxic adenoma . In subclinical hyperthyroidism group (2) patients ,Grave's disease also was the commonest cause in the cases of group (2) 25% .Then come cases with multinodular goiter (16.7%) and only 8.3% of group (2) patients with toxic adenoma .

Table (5) causes of thyroid dysfunction :

		Group				Total		X ²	P
		Overt Hyperthyroidism		Subclinical Hyperthyroidism					
		N	%	N	%	N	%		
Cause	Graves dis.	12	50.0%	0	0.0%	12	25.0%	48	<0.001
	MNG	8	33.3%	0	0.0%	8	16.7%		
	Toxic Adenoma	4	16.7%	0	0.0%	4	8.3%		

Table (6) As regard clinical status at time of examination 79.2% of group (1) patients were complaining of signs and symptoms of hyperthyroidism , and only 20.8 % of them were improved .While in group (2) 66.7% of patients were asymptomatic and the other 33.3 % were symptomatic with Statistical significance between the two groups(p =0.001)

Table (6) : Clinical status in both groups :

		Group				X ² Test	P
		Overt Hyperthyroidism		Subclinical Hyperthyroidism			
		Group (1)		Group (2)			
		N	%	N	%		
Clinical status	asymptomatic	5	20.8%	16	66.7%	10.2	**0.001
	Symptomatic	19	79.2%	8	33.3%		

**p≤0.001 is statistically highly significant

Discussion:

Undiagnosed and untreated hyperthyroidism causes major clinical problems, with negative patient outcomes and rising health-care expenses. As a result, proper diagnosis, classification, careful therapy, and clinical response monitoring of hyperthyroid patients are critical. [6]

Subclinical hyperthyroidism is a less common condition. The reported prevalence in adult populations is between 0.2% to 9.7%, generally about 2% to 3%. It is also more common in women and the elderly.^[7]

So, we shed the light at this study on the value of clinical and biochemical identification of category of hyperthyroidism and correlation with thyroid gland scanning for better management of hyperthyroidism.

Among the 48 patients included in this study 36 /48 (75%) were females and 12/48 (25%) were males with a ratio of [3: 1]. This female predominance in our cases comes in agreement with results of **Ertugrul** study in which females 83 % and the males 17 %^[8].

The median age for all patients in our study was around 41 years old. This comes in agreement with **Ertugrul** study in which median age was 43.6 years.^[8]

Majority of the patients of study were overweight, the median BMI 29.2. On the contrary Ertugrul and Arikan studies documented that most of hyperthyroid patients had average body weight (BMI 24.7 ± 5.8).^[8,9]

In the current study, grave's disease was the commonest cause of hyperthyroid state then multinodular goiter and a small proportion with toxic nodule. There was no significant difference between the two groups of study as regard the cause. As regard thyroid scan evaluation We reported that 83.3% of all group (1) cases had high thyroid uptake , In group (2) patients 62% had high uptake , This comes in agreement with Arikan ,Surks and Alswa studies whom also supported that most common causes of both types of hyperthyroidism was graves' disease
[9,10 ,11]

We reported that most of the patients of overt hyperthyroidism (79%) were symptomatic, all of them had abnormal thyroid examination and 50% had thyroid eye disease .On the contrary most of subclinical hyperthyroidism (66.7%)cases were asymptomatic ,50 % of them presented with abnormalities in thyroid examination and only 34 % with thyroid eye disease .This comes in

agreement with Surks study who noticed that patients with subclinical hyperthyroidism had minor clinical symptoms and signs than overt hyperthyroid.^[10]

We reported that there was highly statistical significant variation between the two groups as regard F. T4(P = <0.001) and also F .T3 (p = <0.001), but no significant difference in TSH(p =0.223) .TSH was below reference range in both groups but free T4and free T3 were increased only in group (1) overt hyperthyroid patients .this comes in accordance with Surks study results .^[10]

Conclusion:

In view of the present study we can conclude: Hyperthyroidism is highly prevalent in females than males. Overt hyperthyroid patients had more symptoms and signs than subclinical hyperthyroidism. Thyroid scan had an important role in determination of the cause of hyperthyroidism

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Availability of data and materials: All analyzed and generated data through this study are incorporated in this published article.

Consent for publication

An informed written consent had been taken from all participating patients to publish their data.

Competing interests: The authors announce that having no compete

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