

## Clinical study of cases with hyperthyroidism in Erbil Governorate, Kurdistan Region-Iraq

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### Abstract

**Background and objectives:** Thyrotoxicosis is a common and serious world-wide health problem, it's one of the common problems in Erbil governorate.

**Methods:** Clinical analysis done for 675 patients proved to have thyrotoxicosis by thyroid function tests.

**Results:** Hyperthyroidism in females were 4 times more common than in males, the mean age was around 44 years, graves disease being the most common cause, followed by multinodular goiter, Iodine-induced thyrotoxicosis , single nodule goiter, T3-Thyrotoxicosis, then finally auto-immune lymphocytic thyroiditis. Weight loss was the most common feature, followed by other well known features of autonomic hyperactivity, tremor was the most common sign reported while periodic paralysis was the least common sign.

**Conclusion:** Graves disease is the commonest cause of thyrotoxicosis. Iodination of salt program resulted in transient increase and later on decrease of thyrotoxicosis in the region.

**Key words:** Hyperthyroidism; Thyrotoxicosis, Graves disease

### Introduction

Hyperthyroidism is a heterogeneous group of disorders all characterized by elevated levels of free (non-protein-bound) thyroid hormones in the blood<sup>1</sup>. It's a common endocrinological disorder with a prevalence of about 20/1000 females; males affected five times less frequently<sup>2</sup>. Most of the cases are either due to Graves' disease which is associated with a diffuse goiter, or due to multinodular or uninodular goiter<sup>1,2</sup>. Several myopathic diseases are related to hyperthyroidism: Chronic thyroid myopathy, Exophthalmic ophthalmoplegia (Graves' ophthalmopathy), Periodic paralysis, Myasthenia Gravis associated with thyrotoxicosis<sup>3</sup>. Clinical manifestations of thyrotoxicosis are due to the direct physiologic effect of the thyroid hormones, as well as to the increased sensitivity to catecholamine

causing tachycardia, tremor, stare, sweating and lid lag<sup>4</sup>. Females are affected 5-times more than males between the 3<sup>rd</sup> & 5<sup>th</sup> decade of life. It's one of the common endocrine disorders in Iraq. Symptoms of hyperthyroidism includes: Nervousness, excessive sweating, hypersensitivity to heat, palpitation, fatigue weight loss, tachycardia dyspnea, weakness, increase appetite, eye complaints, swelling of legs, diarrhea, and anorexia<sup>4</sup>. Signs of hyperthyroidism includes: Tachycardia, goiter, skin changes, pretibial myxedema, oncholysis, tremor, eye signs, AF, splenomegaly, palmar erythema, bruit over the thyroid, hot hands, moist hand, Lid retraction, Lid lag, hyperkinetic movements<sup>4</sup>. Three treatment modalities are used to control hyperthyroidism: Medical, Surgical, and Radioactive iodine. Anti-thyroid drugs commonly used includes: Propylthiouracil, Methimazole, &

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Carbimazole<sup>1</sup>. Elevated free T4 & a suppressed TSH confirm the clinical diagnosis of thyrotoxicosis. TSI is usually elevated and is especially useful in patients with eye signs who do not have other characteristic clinical features. Increased uptake of iodine (123) differentiates Grave's disease from early subacute or Hashimoto's thyroiditis in which uptake is low in the presence of hyperthyroidism<sup>1</sup>. Unsuspected & undiagnosed hyperthyroidism arose in roughly 0.5% of women in a large population-based British survey done in the 1970s<sup>5</sup>. In a more recent survey done in the USA, investigators noted hyperthyroidism in 0.5% of randomly selected individuals. An additional 0.8% had subclinical or mild hyperthyroidism, in which serum thyrotropin is low or undetectable, but circulating thyroid hormone is within the normal range<sup>6</sup>. The development of the various forms of hyperthyroidism depends to a great extent on the iodine intake of the population. For example, an epidemiological survey compared an area of normal iodine intake (Iceland) & an area of low iodine intake (East Jutland, Denmark). Graves' disease accounted for at least 80% of new cases of hyperthyroidism in Iceland, whereas toxic multinodular or uninodular goiter caused over half the new cases in Denmark. Further, the incidence of all cause of hyperthyroidism was lower in Iceland than in Denmark (about 40 cases per 100 000 per year vs. about 25 cases per 100 000 per year)<sup>5</sup>. This study aimed to explore the epidemiology and clinical presentations of cases with thyrotoxicosis managed as an outpatient clinics or inpatients in Erbil teaching hospitals (Erbil & Rizgary).

## Methods

Patients with diagnosis of hyperthyroidism based on clinical and hormonal study presented to the outpatient clinics in Erbil & Rizgary Teaching Hospital, and patients from private clinic during a period of 12 years (144-months) were evaluated clinically and medical treatment given to them with 6-monthly follow up depending on the

program of monthly medical treatment supply in the hospital for the clinical patterns of the illness and response to medical treatment for 18-months. All patients who were diagnosed as hyperthyroidism from January 1998 to January 2010 were prospectively studied. Complete physical and neurological examination done to them by a Physician and Neurologist. Hormonal study: T3, T4, and TSH, were done for all of them to prove the diagnosis<sup>1</sup>. After one month the hormonal study was repeated to see the response to the medical treatment and then every 6-months, and later on after 18-months when medical treatment was planned to stop. Monthly follow up of the patient in Rizgary Teaching Hospital, and private clinic have been done depending on the program of medical treatment supply (Neomercazole, and, Propranolol) in the Hospital. The differences in: age, sex, and underlying cause (Graves' disease, multinodular goiter, uninodular goiter, etc.) have been studied. The results of the study was related to the role of iodizing table salt program which play an important role in prevention of goiter and eventually prevention of hyperthyroidism in our locality. Comparison of the results with the other studies else where has been done. The patient with normal thyroid function tests namely normal thyroxine (T4) & triiodothyronine (T3) were excluded from the study, also those with subclinical hyperthyroidism were excluded, while patients who were proved to have thyrotoxicosis by thyroid function tests namely elevated thyroxine (T4), and/or tri-iodothyronine (T3) and low TSH were entered in the study for the analysis of their age, sex, smoking status, cause of thyrotoxicosis, symptoms, signs, eye manifestations. The thyroid function tests were carried out by the Mini Vidas ELFA (enzyme linked fluorescent assay) method and immunoradiometric assay (IRMA). A verbal consent was obtained from all participants, they were informed about the investigation required for the study and the purpose behind it. The data have been processed by the use of statistical package of social

science version 15 for windows (SPSS) software. The different groups and sub-groups computed for statistical evaluation as the number and percent of patients affected by thyrotoxicosis utilizing the Chi-square test. The age factor, duration of disease in years, and number in each group all evaluated by Chi-square test for terms of comparison (observed versus expected frequencies).

## Results

Table (1), shows the number of patients presented with thyrotoxicosis yearly from 1998 – 2010 and gender difference in each year. It shows that most cases were seen during the years 1998 & 1999, while the lowest number was in the years 2008 & 2009. It also shows that females were 4

times affected more than males. Table (2), shows the age distribution of the patients, indicating that the age range was from 16 to 75 years of age & the mean age affected was around 43 years age. Table(3), Shows the etiology of thyrotoxicosis, Graves disease was the most common cause, followed by multinodular goiter, single nodule goiter, Iodine-induced & lastly autoimmune lymphocytic thyroiditis. Table (4), shows the symptoms manifestations of the cases in this series. Weight loss was the most common feature, followed by other well known features of autonomic hyperactivity. Table (5), shows the sequences of reported signs among patients. Tremor was the most common sign while familial periodic paralysis was the least one.

**Table 1:** Total number of patients with thyrotoxicosis during the 12-years of study.

The Years	Female No. (%)	Male No. (%)	Total No.
1998	63 (84%)	12 (16%)	75*
1999	60 (72%)	23 (28%)	83*
2000	51 (84%)	10 (16%)	61*
2001	64 (76%)	20 (24%)	84*
2002	72 (86%)	12 (14%)	84*
2003	24 (80%)	6 (20%)	30
2004	35 (83%)	7 (17%)	42
2005	27 (66%)	14 (34%)	41
2006	34 (76%)	11 (34%)	45
2007	44 (76%)	14 (34%)	58
2008	25 (68%)	12 (32%)	37
2009	30 (86%)	5 (14%)	35
<b>Total</b>	<b>529 (78%)</b>	<b>146 (22%)</b>	<b>675</b>

\*P-value<0.05

**Table 2:** Age distribution of patients with thyrotoxicosis with the mean age.

	Female	Male
Age Range	16 to 78 Years	18 to 70 Years
Mean Age	43.587	40.253

**Table 3:** Etiology of thyrotoxicosis in studied patients .

Cause	No. of Cases	Percentage of Total
Grave's disease with diffuse goiter	428	63.4%
Multinodular goiter	140	20.7%
Iodine induced	51	7.6%
Single nodule	42	6.3%
T3-thyrotoxicosis	12	1.78%
Auto-immune lymphocytic thyroiditis	2	0.3%
<b>Total</b>	675	100.0%

**Table 4:** Sequences of presenting symptoms in patients with thyrotoxicosis.

Symptoms	No. of cases	Total%
Weight loss	375	55.6%
Palpitation	265	39.2%
Increased appetite	203	30%
Increased sweating	166	24.6%
Heat intolerance	154	22,8%
Nervousness	122	18%
Dyspnea on exertion	85	12.6%
Decreased appetite	96	14.2%
Hyper defecation	69	10.3%
Muscle weakness	60	8.9%
Fatigue	54	8%
Diarrhea	35	5.2%
Myalgia	33	4.93%
Family history	36	5.33%
Insomnia	22	3.3%
Arthralgia	19	2.8%
Pruritus	17	2.5%
Alopecia	15	2.2%
Vomiting	13	1.92%
Constipation	9	1.33%
Bone pain	4	0.06%
Ankle edema	4	0.06%

**Table 5:** Signs of patients with hyperthyroidism.

Signs	No. of cases	Total%
Tremor	465	68.88%
Wide pulse pressure	243	36%
Sinus tachycardia	232	22.56%
Hyper-reflexia	149	10.84%
Proximal myopathy	97	8.18%
Heart failure	88	6.19%
AF	56	5.08%
Cardiomyopathy	39	3.98%
Vitiligo	21	2.43%
Palmer erythema	15	1.54%
Pigmentation	12	1.32%
Splenomegaly	10	1.10%
Digital clubbing	9	0.66%
Spider naevi	7	0.66%
Onycholysis	5	0.66%
Pretibial myxedema	5	0.44%
Familial periodic paralysis	3	0.22%

## Discussion

Table (1) shows that most cases were seen during 1998 & 2002, this can be attributed to a program of iodination of table salt sponsored by UNICEF in collaboration with DOH in Erbil (In relation to SCR-986, Oil for Food Program) giving and educating the people to use Iodine supplements in the salt to help prevent goiter in the community which is a risk factor in increasing the incidence of thyrotoxicosis by the well-known Jod-Basedo phenomenon, in this issue females were approximately four times more affected than males. In a study done for 203 patients seen at King Abdulaziz University Hospital, Saudi Arabia. the female: male ratio was 3.8:1 & mean age of 35.49+/-10.86 year. These results were comparable to our results<sup>7</sup>. Graves' disease was the underlying cause in 65% of cases, toxic multi nodular goiter in 20.7%, and toxic adenoma and sub acute thyroiditis in 7.6% and 6.3% respectively 1%. Palpitations, tremor, weight loss and nervousness

were the commonest presenting manifestations. Fifty-five (55%) of patients were treated with antithyroid drugs, 15% with radioactive iodine and 30% underwent subtotal thyroidectomy. Post radiotherapy hypothyroidism developed in 25% of patients<sup>5</sup>. Table(2), shows the age distribution of the cases, indicating that the age range was from 16-75 years of age & the mean age affected was around 43 years age. In a study from Olmsted County, Minnesota, USA, the peak incidence rates were bimodal, occurring in the age groups 40-44 years & 60-64 years in females & 45-49 years & 65-69 years in males<sup>8</sup>. Table(3) Shows the aetiology of thyrotoxicosis, graves disease being the most common cause, followed by multinodular goiter, single nodule goiter, Iodine-induced, T3-thyrotoxicosis then finally auto-immune lymphocytic thyroiditis. In a recent study from Germany, thyrotoxicosis was one of the most common endocrine disorders, affecting 2% of the adult population. Graves' disease & its variants are the most

frequent cause. The prevalence of toxic nodular goiter & toxic adenoma is increased in areas of limited iodine supply. Thyrotoxicosis in patients with multinodular goiter can be precipitated by iodinated radiocontrast agents & the antiarrhythmic drug amiodarone. Transient hyperthyroidism may be caused by HCG-induced thyroiditis in pregnancy or de Quervain subacute thyroiditis<sup>9</sup>. These data are going with our results. Table(4), shows the symptomatic presentations of the cases in this series, indicating that weight loss was the most common feature, followed by other well known features of autonomic hyperactivity. Interestingly it shows that decreased appetite was more common than increased appetite. Clinical manifestations of thyrotoxicosis range from silent to florid & can mimic those of other conditions occurring in pregnancy and old age. The diagnosis may be particularly vexing in elderly patients with apparent dementia. Once clinical suspicion has been aroused, the workup to confirm the diagnosis & establish the cause is easily accomplished<sup>10,11</sup>. A study from Nigeria showed that the presence of a goiter, ocular changes, high sleeping pulse rate, fine silky-smooth skin & thin, short & scanty hair have been identified as important clinical clues to look for to aid in the diagnosis of a difficult case in an environment where there are no facilities for thyroid function tests.<sup>12</sup> Table (5), shows the reported signs manifested by our cases. The tremor was the most common sign reported while familial periodic paralysis was the least common sign. Typical symptoms of hyperthyroidism indicate the action of excess thyroid hormone in the cell, as well as enhanced adrenergic activity. Patients usually have fatigue, nervousness or anxiety, weight loss, palpitations, and heat-sensitivity. Women might have irregular menses & decreased fertility, although frank amenorrhoea is rare<sup>13-15</sup>. About 15% of elderly individuals with new onset atrial fibrillation have thyrotoxicosis<sup>16,17</sup>. Conversely, a high proportion (as many as 25–35%) of elderly people with thyrotoxicosis will develop atrial

fibrillation that is resistant to treatment until the underlying thyroid disorder has been corrected<sup>18</sup>. Other indicators of hyperthyroidism include osteoporosis, hypercalcaemia, congestive heart failure, premature atrial contractions or atrial fibrillation, shortness of breath, muscle weakness, anxiety. In older patients, weight loss might be accompanied by anorexia rather than increased caloric intake, prompting an often extensive, expensive, ultimately unsuccessful search for hidden malignant disease<sup>19</sup>. Hypokalaemic periodic paralysis, typically seen in thyrotoxicosis in Asian men might be due to concomitant mutations in genes coding for potassium channels in muscle<sup>3</sup>. Elderly individuals have less obvious symptoms and signs than younger patients, including a lower frequency of goiter and a higher prevalence of cardiac manifestations such as atrial fibrillation and, more rarely, congestive heart failure.

## Conclusion

Graves disease is the commonest cause of thyrotoxicosis. Iodine induced thyrotoxicosis was observed to be an important cause of thyrotoxicosis in Erbil during the period (1998-2010). Weight loss with increased appetite and palpitation are the commonest symptoms while tremor and wide pulse pressure are the commonest signs.

## References

1. Peter A. Singer, et al, Treatment guidelines for patients with hyperthyroidism and hypothyroidism, *JAMA Middle East*, Vol. V, June No.6, 1995; 35-39.
2. Tunbridge WM, Evered DC, Hall R, et al. The spectrum of thyroid disease in the community: the Wickham survey. *Clin Endocrinol (Oxf)* 1977; 7: 481-93.
3. Raymond's D. Adams, Principles of Neurology, Maurice Vector, 6<sup>th</sup> edition, 1998: Chapter: 15: pp. 1233-1234.
4. M. W. J. Strachan, B. R. Walker, Endocrine disease: Thyrotoxicosis, Clinical features, Davidson's principles and practice of medicine, 20<sup>th</sup> edition. 2006: Chapter: 20; pp. 739-804.

5. David S Cooper. Seminar: hyperthyroidism. THE LANCET • Vol 362 • August 9, 2003;459-68.
6. Trzepacz PT, Klein I, Roberts M, Greenhouse J, Levey GS. Graves' disease: an analysis of thyroid hormone levels and hyperthyroid signs and symptoms. *Am J Med* 1989; 87: 558–61.
7. Akbar DH, Mushtaq MM, Al-Sheik AA5. Etiology and outcome of thyrotoxicosis at a university hospital, Saudi Med J. 2000 Apr;21(4):352-4.
8. Bartley GB6. The epidemiologic characteristics and clinical course of ophthalmopathy associated with autoimmune thyroid disease in Olmsted County, Minnesota, *Trans Am Ophthalmol Soc.* 1994;92:477-588.
9. Henzen Ch7. Hyperthyroidism--differential diagnosis and differential therapy, *Schweiz Rundsch Med Prax.* 2003 Jan 8;92(1-2):18-24.
10. Mazzaferri EL8. Recognizing thyrotoxicosis. *Hosp Pract (Minneap).* 1999 May 15;34(5):43-6, 49-51, 55-6 passim.
11. Gilkison CR9. Thyrotoxicosis. Recognition and management. *Lippincotts Prim Care Pract.* 1997 Nov-Dec;1(5):485-98.
12. Famuyiwa OO, Bella AF10. Thyrotoxicosis in Nigeria. Analysis of a five year experience. *Trop Geogr Med.* 1990 Jul;42(3):248-54.
13. Krassas GE. Thyroid disease and female reproduction. *Fertil Steril* 2000; 74: 1063–70.
14. Carlson H. Gynecomastia. *N Engl J Med* 1980; 305: 795–99.
15. Dias Da Silva MR, Cerutti JM, Arnaldi LA, Maciel RM. A Mutation in the KCNE3 potassium channel gene is associated with susceptibility to thyrotoxic hypokalemic periodic paralysis. *J Clin Endocrinol Metab* 2002; 87: 4881–84.
16. Cobler JL, Williams ME, Greenland P. Thyrotoxicosis in institutionalized elderly patients with atrial fibrillation. *Arch Intern Med* 1984; 144: 1758–60.
17. Trivalle C, Doucet J, Chassagne P, et al. Differences in the Signs and Symptoms of Hyperthyroidism in Older and Younger Patients. *J Am Geriatr Soc* 1996; 44: 50–53.
18. Shimizu T, Koide S, Noh JY, Sugino K, Ito K, Nakazawa H. Hyperthyroidism and the management of atrial fibrillation. *Thyroid* 2002; 12: 489–93.
19. Ronnov-Jessen V, Kirkegaard C. Hyperthyroidism: a disease of old age? *BMJ* 1973; 1: 41–43.