

# Histological study the incidence thyrotoxicity between men and women of AL- Ramadi city

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## Abstract

*Thyrotoxicosis is the clinical manifestation of excess thyroid hormone action at the tissue level due to inappropriately high circulating thyroid hormone concentrations. Hyperthyroidism, a subset of thyrotoxicosis, refers specifically to excess thyroid hormone synthesis and secretion by the thyroid gland. This study aims to show the differentiate between men and women affected with thyrotoxicity in different ages and study the histological changes with hormonal evaluation. This study was done using 50 patients with hyperthyroidism. ( 25 women and 25 men ) Patients have been taken from Arrazzi private hospital and Al-Ramadi hospital . Hormonal testes (TSH, T3, T4) was collected and recorded. Information of patents: Name, Age and gender was recorded. the pathological samples of thyroidectomy were collected after operation and saved it in 10% Formalin for Histopathological stud. A significant ( $p < 0.05$ ) increases in thyroid hormone (T3 & T 4) in women more than men. Slides showed a diffuse area of hemorrhage and diffuse inter follicular lympho-neutrophilic infiltration was seen in the tissue. The results of the study reflected that the incidence of thyrotoxicity more effective in women than men.*

**Keywords:** Thyrotoxicity, thyroid hormones. Hyperthyroidism. Histology.

## Introduction

Hyperthyroidism is a pathological disorder in which excess thyroid hormone is synthesized and secreted by the thyroid gland. It is characterized by normal or high thyroid radioactive iodine uptake (thyrotoxicosis with hyperthyroidism or true hyperthyroidism). Thyrotoxicosis without hyperthyroidism is caused by extrathyroidal sources of thyroid hormone or by a release of preformed thyroid hormones into the circulation with a low thyroid radioactive iodine uptake[11]. Hyperthyroidism can be overt or subclinical. Overt hyperthyroidism is characterized by low serum thyroid-stimulating hormone (TSH) concentrations and raised serum concentrations of thyroid hormones: thyroxine (T<sub>4</sub>), tri-iodothyronine (T<sub>3</sub>), or both. Subclinical hyperthyroidism is characterized by low serum TSH, but normal serum T<sub>4</sub> and T<sub>3</sub> concentrations. [5] With recent advances in psych neuroendocrinology, there has been growing interest in the psychological aspects of clinical care

in endocrine disease. Thyroid disorders have long been associated with psychiatric illness, often with symptoms suggestive of mood disorders. The most common clinical features associated with hyperthyroidism have been anxiety and depression.[20]

Bipolar disorders, especially bipolar mania, is less commonly documented.[29] Studies have shown that mood disturbance often accompanies hyperthyroidism in patients. [16] Substantial numbers of patients with hyperthyroidism exhibit features of depressive disorders.[25] and some patients with hyperthyroidism develop mania-like symptoms.[13] Such patients can be diagnosed with mood disorders due to hyperthyroidism because the symptoms of depressive and bipolar disorders are the direct physiological effects of hyperthyroidism, according to the criteria of the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV).

Prospective studies investigating the effect of successful treatment of hyperthyroidism on mood disturbance showed that both mood disturbance and hyperthyroid symptoms subsided equally with the treatment.[25] There is no doubt that elevated thyroid hormone level has direct effect on mood. However, we can also hypothesize that a history of hyperthyroidism increases the risk of subsequent onset of "idiopathic" bipolar disorder.

Hyperthyroidism is more common in women than men (5:1 ratio). The overall prevalence of hyperthyroidism, which is approximately 1.3 percent, increases to 4 to 5 percent in older women. Hyperthyroidism is also more common in smokers. Graves' disease is seen most often in younger women, while toxic nodular goiter is more common in older women. [9] Hyperthyroidism increases with age and is more frequent in women. The prevalence of overt hyperthyroidism is 0.5–0.8% in Europe, and 0.5% in the USA. Data for ethnic differences are scarce, but hyperthyroidism seems to be slightly more frequent in white people than in other races.[35] The incidence of mild hyperthyroidism is also reported to be higher in iodine-deficient areas than in iodine-sufficient areas and to decrease after introduction of universal salt iodization programmes.[ 34]

The most common causes of hyperthyroidism are Graves' disease, followed by toxic multinodular goiter, whilst rarer causes include an autonomously functioning thyroid adenoma or thyroiditis. In epidemiological studies, however, the aetiology is rarely ascertained. The prevalence of hyperthyroidism in women is between 0.5 and 2% and is 10

times more common in women than in men in iodine-replete communities.[ 12] In NHANES III, in those subjects who were neither taking thyroid medication nor reported histories of thyroid disease, 2 per 1000 had ‘clinically significant’ hyperthyroidism, defined as a serum TSH concentration < 0.1 mIU/l and a serum total T<sub>4</sub> concentration > 170 nmol/l.[26] The prevalence data in elderly persons show a wide range between 0.4 and 2.0% [14], [1], [18] and a higher prevalence is seen in iodine-deficient areas[37],[36].

Subclinical hyperthyroidism is defined as a low-serum TSH concentration and normal serum T<sub>4</sub> and T<sub>3</sub> concentrations, in the absence of hypothalamic or pituitary disease, non-thyroidal illness or ingestion of drugs that inhibit TSH secretion such as glucocorticoids or dopamine[12].

Epidemiological studies differ in the definition of a low serum TSH concentration and whether the subjects included were receiving levothyroxine therapy. The reported overall prevalence is 3%, with men and women over 65 years having the highest prevalence with 50% taking levothyroxine. In the NHANES III study the prevalence was highest in those subjects aged 20–39 years and those aged > 79 years. In this study, the percentage of subjects with serum TSH concentrations < 0.4 mIU/l was significantly higher in women than in men and black subjects had significantly lower mean serum TSH concentrations and therefore a higher prevalence of subclinical hyperthyroidism (0.4%) than whites (0.1%) or Mexican Americans (0.3%). The prevalence of subnormal serum TSH concentrations is higher in iodine-deficient populations (6-10%), due to functional autonomy from nodular goiters [12].

The prevalence and incidence increased with age and were two-fold higher among women than men. Women also showed two distinct peaks in incidence at the age of 30 and 50; after the age of 60, the trend became similar between sexes. With regard to the geographic distribution, an

increasing gradient of incidence was observed from the northern to the south-western areas of the Region.[8]

To prove our hypothesis, we designed a nationwide population-based study to investigate the actual incidence of bipolar disorders in patients with hyperthyroidism in Al-Ramadi city.

## Material and Methods

This study was done using 50 patients with hyperthyroidism. ( 25 women and 25 men ) Patients have been taken from Arrazy private hospital and Al- Ramadi hospital. Hormonal testes (TSH, T<sub>3</sub>, T<sub>4</sub>). Information of patents: Name, Age and gender was recorded. the pathological samples of thyroidectomy were collected after operation and saved it in 10% Formalin for Histopathological study and normally using mechanized tissue processor (Leica TP1020). The method of hormonal assessment were done according to the company instructions ( Biomeriux company).

**Statistical Analysis:** The Statistical Analysis System–SAS was used for the analysis of data and to determine the significance the incidence Thyrotoxicity between men and women of Al-Ramadi city according to the Completely Randomized Design-CRD and compared the significant differences between men and women by Least Significant Differences (LSD), with a nature probability (highly in women).

## Results

**Hormonal changes:** The results of statistical analysis (Table 1, Figure 1) showed significant ( $p \leq 0.05$ ) differences. hyperthyroidism in women and men compare with healthy people especially high levels of T<sub>3</sub> and T<sub>4</sub> in women, most commonly indicate a condition called Grave’s disease. It’s an autoimmune disorder associated with hyperthyroidism. Table 2 showed the gender. A significant incidence in women compare with men.

**Table 1**  
Shows concentration of thyroid hormones between people which suffering hyperthyroidism man and women compare with healthy people.

Patient	type of test	Mean	Std. Deviation
Man	T3	3.700	.1581
	T4	9.480	.4604
	TSH	0.876	.1278
	Total	4.685	3.7164
Women	T3	7.020	.8136
	T4	16.000	1.2247
	TSH	1.300	.4082
	Total	8.106	6.2548
Control	T3	2.360	.2302
	T4	5.400	1.1402
	TSH	1.783	2.5965
	Total	3.181	2.2907

Table 2

Multiple Comparisons between the gender people which suffering hyperthyroidism man and women and healthy people

Dependent Variable: Concentration of test LSD						
(I) patient	(J) patient	Mean Difference (I-J)	Std. Error	Sig.	95% Confidence Interval	
					Lower Bound	Upper Bound
Man	women	-3.908*	.4348	.000	-4.789-	-3.026-
	control	1.592*	.4205	.001	.739	2.444
women	Man	3.908*	.4348	.000	3.026	4.789
	control	5.499*	.4282	.000	4.631	6.367
control	Man	-1.592*	.4205	.001	-2.444-	-.739-
	Women	-5.499*	.4282	.000	-6.367-	-4.631-

- Based on Observed Means.
- The error term is Mean Square (Error) = 1.369.
- The Mean Difference is significant at the .05 level.

Histopathological observations

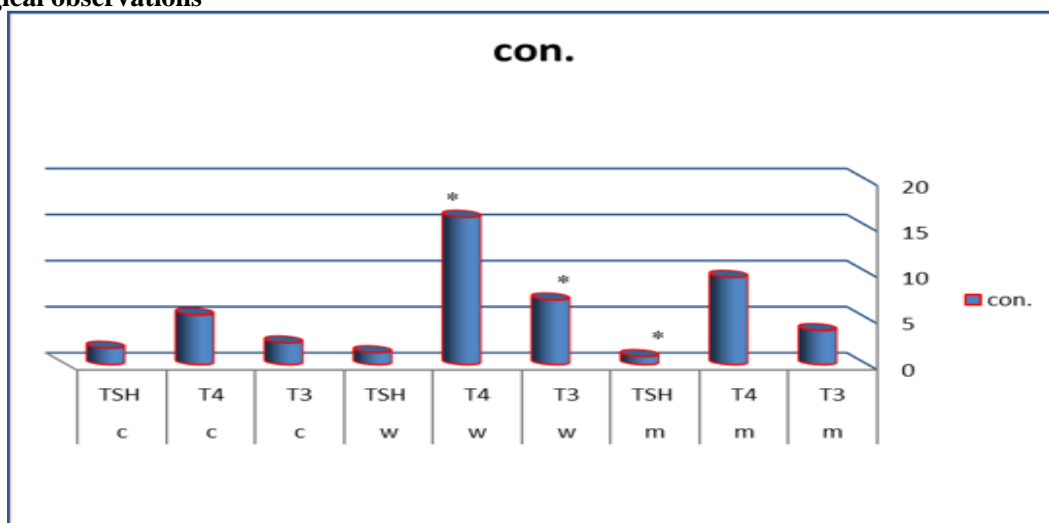


Figure 1: Concentration of thyroid hormones between people which suffering hyperthyroidism woman and man compare with healthy people (95% Confidence Interval)

Histological observation

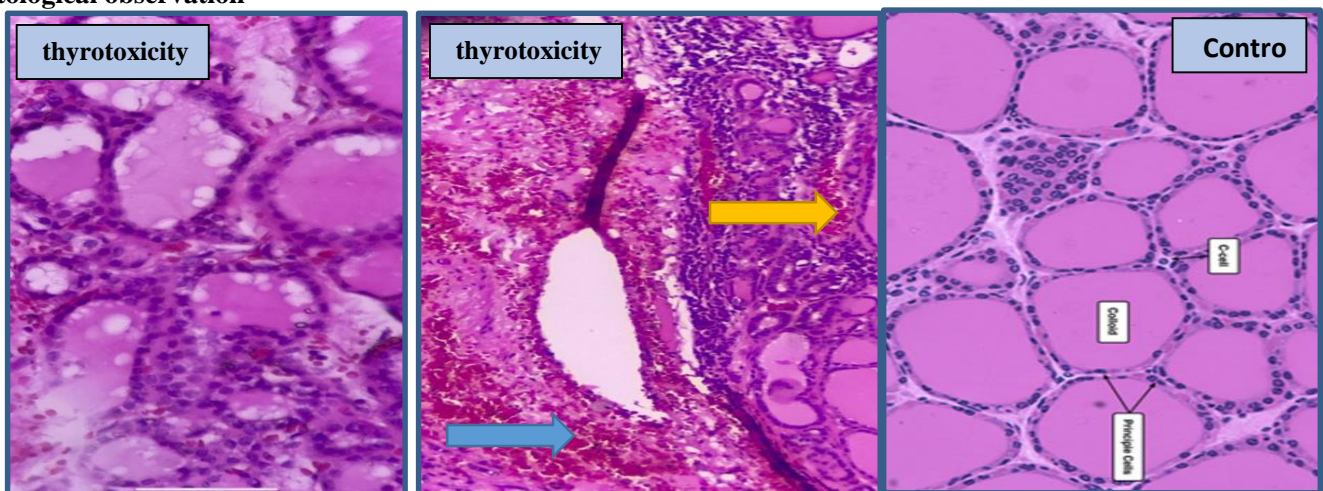


Figure 2: Numerous sized thyroid follicles containing colloid with numerous vacuoles (fat). Black Arrow: A diffuse area of hemorrhage was seen in the adjacent tissue. Blue Arrow: Extensive area of follicular atrophy with areas of hyperemia and diffuse inter follicular lympho-neutrophilic infiltration was seen. Yellow Arrow: A wide area of follicular scalloping with colloid accumulation was also observed. Active lymphocytic thyroiditis as compare with Control slide.(H&E) 40x

## Discussion

Based on the available data we assumed. There is an increase in the hormones T4 and T3 in women than in men. Thyrotoxicity in women is much higher than that in men, so estrogen plays a key role in the development of thyroid cancer. Estrogen plays its growth-promoting role through classical genomic and non-genomic pathways mediated by membrane-bound estrogen receptors. We summarize the understanding of molecular mechanisms of estrogen signaling pathways in thyroid cancer. Furthermore [31] no strong link between the use of fertility drugs and thyrotoxicity incidence, we observed a modest increased thyrotoxicity incidence after the use of progesterone [30]. In patients with silent thyroiditis, post-partum thyroiditis, or subacute painful thyroiditis, the destruction of thyrocytes leads to release of preformed hormones into the circulation. [19,20]. Drug-induced thyrotoxicosis has the same pathogenic mechanism as thyroiditis. Lithium, interferon  $\alpha$  and amiodarone are commonly involved in drug-induced thyroid dysfunction. Postpartum thyroiditis is an autoimmune disease and associated with the presence of antibodies to thyroid peroxidase (TPO). Chances of developing postpartum thyroiditis in pregnant women who have positive TPO antibodies early in pregnancy are 30% to 52%. Postpartum thyroiditis could occur after the loss of a pregnancy at 5 to 20 weeks gestation [28]. Diagnosing postpartum thyroid dysfunction is challenging, because symptoms may be subtle. A team approach involving primary care providers, endocrinologists and obstetricians is essential for transitioning thyroid care from the gestational to the postpartum setting [7]. Women with FNAH and mild thyrotoxicosis prior to pregnancy may have continuous hyperthyroidism with additional change due to the series of human chorionic gonadotropin secretion during pregnancy. A number of scientists have found in their research that the physiological changes in the economy of thyroid hormone that occur during pregnancy, especially in the first trimester of pregnancy. Approximately one to two cases of hyperthyroidism occur per 1,000 [38].

Scientists have shown that iodine is a micronutrient necessary for the production of thyroid hormones. Chronic thyroid stimulation leads to an increased prevalence of toxic nodular goiter and hyperthyroidism in the population. This high prevalence of nodular independence usually leads to a further increase in the prevalence of hyperthyroidism if iodine intake is subsequently increased by salt iodization [6].

Pregnant and breastfeeding women have been found to have higher iodine needs than other adults; The intake ranges from 220 to 250 mcg/day during pregnancy and from 250 to 290 mcg/day during lactation [24]

This is because of iodide pool reduces during pregnancy because of increased renal clearance of iodine and transfer of iodine to the feto-placental unit. This results in an additional requirement of iodine during pregnancy of ~100%

as compared to nonpregnant adults. In accordance, the recommended iodine intake in pregnancy is 250  $\mu\text{g/day}$  [4].

We conclude that its excessive intake leads to hyperthyroidism by exceeding the specified dose and that its deficiency leads to hypothyroidism of the thyroid gland. Studies have shown that cigarette smoking has multiple effects on the thyroid gland. Smoking appears to cause changes in thyroid function tests, such as decreased TSH and increased thyroid hormones. Researchers have found that Graves' disease is the most common cause of persistent hyperthyroidism in adults. About 3% of women and 0.5% of men will develop Graves' disease during their lifetime [17]

Several studies have confirmed a significant effect of smoking on Graves' hyperthyroidism and especially on Graves' orbitopathy. Here, smoking may increase the risk of disease development, may reduce the effectiveness of treatment and eventually cause a relapse [24] smoking was associated with a decreased risk of incident thyroid cancer in men but not in women and this association was observed even after adjusting for TSH and BMI levels as potential mediators [2] pregnant women as reflected by a high triiodothyronine (T3)/thyroxine (T4) ratio. We speculated how maternal adiposity and smoking would associate with different thyroid function tests in the early pregnancy [3]. Smoking mainly led to a decrease in TSH levels and an increase in triiodothyronine (T3) and thyroxine (T4) levels, while BMI levels were positively correlated with TSH and free T3 levels. Excess iodine led to an increase in TSH levels and a decrease in thyroid hormone levels. [22]

Studies have found that people are mostly exposed to thiocyanate through diet and cigarette smoke. Thiocyanate is a possible thyroid disorder due to its ability to block iodide uptake by the thyroid gland. Thiocyanate also interacts with enzymatic reactions associated with iodide formation and thyroid hormone synthesis. Both serum thyroid-stimulating hormone and T3 are typically increased in obese compared with lean individuals [19]. Rare causes of hyperthyroidisms are as follow: pituitary adenoma, autoimmune thyroiditis (Hashitoxicosis), levothyroxine overdose, inadequate iodine supplementation (including amiodaron induced hyperthyroidism, iodine-based contrast media), hCG excess (pregnancy, gestational trophoblastic disease, germ-cell tumors. Lithium salts may cause the development of goiter, hypothyroidism, or rarely hyperthyroidism. [10]

We reviewed the literature assessing the associations between thyroid disease and sleep disorders and noted that hyperthyroidism and hypothyroidism have clinical overlap with sleep conditions such as insomnia, restless legs syndrome and obstructive sleep apnea. These findings highlight the importance of identifying and managing thyroid dysfunction for patients with these common sleep disorders [10]

Recent evidence has demonstrated an association between low vitamin D status and autoimmune thyroid diseases such as Hashimoto's thyroiditis and Graves' disease. Thyroid hormones are essential during infancy and childhood for growth and brain development. Graves' disease, Hashimoto's thyroiditis, subacute, painless and postpartum thyroiditis, have been reported as a complication of COVID-19 and causality by the virus has been strongly implicated in all of them. Similar thyroid problems have been reported in the past with the SARS-CoV outbreak in 2002[27]

## Conclusion

In conclusion, it seems that the prevalence and incidence of hyperthyroidism among the general population in Al-Ramadi city is similar to other regions of the world. We recommend conducting well-designed surveys with enough geographic disparity about the epidemiologic characteristic of thyroid dysfunction in Al-Ramadi city that could provide a better picture of age, sex, trend and geographic distribution of hyperthyroidism. The diagnostic and drug-prescription rates of the overt hyperthyroidism were less than 50% of affected patients and were lower than the rates observed in developed countries. Whereas, the healthcare indices in Al-Ramadi city were improved in recent years and further studies to reevaluate these rates are needed, the 'policy makers' attention is essential to improved diagnostic rate of thyroid dysfunctions.

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