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Correlation of histological changes with IgG and thyroid hormone concentrations in nodular toxic goiter patient's.

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Abstract

Background : Thyroid disease includes many physiological disorders Toxic nodular goiter one of these disease involves an enlarged thyroid gland that reflex rounded growths called nodules. These nodules is abnormal and produce too much thyroid hormone.

Methods: This study was conducted to determinate the macroscopical and microscopical changes occurring in thyroid gland affected with toxic nodular goiter of both sexes, males and females. A total number of patients was 80 patients. 15 patients out of 80 were affected with nodular toxic goiter (2 male and 13 female).

Results: Macroscopical examination showed the presence of mono and multinodular lesion with hypertrophy of some follicles and atrophy for other. Calcifications, haemorrhage, bundles of fibers were found with the matrix of thyroid tissues. Concerning microscopical examinations, it had been found that appearance of lymphoid nodules, cellular hypertrophy, hyperplasia and increase number of follicles cysts. Measurements of epithelium, colloid and follicles diameter were significantly ($P<0.05$) taller than healthy tissues. These changes might be attributed to continuous stimulating effects of thyroid which interne increase the activity of gland and tissues hypertrophied.

Conclusion :Presence of various form of toxic goiter nodules correlated with many histological and hormonal alterations in addition to enhancements of antibody concentration .

Key words: nodular goiter , hyperplasia , fibrosis .TSH. IgG

Introduction:

Thyroid gland is the largest endocrine glands of the body and exerts main vital role in the functioning of the most body cells. It secrets two important active metabolic hormones (Triiodothyronine T3 and Tetraiodothyronine T4) (1). Goiter, hypothyroidism, hyperthyroidism and tumors are the most common thyroid diseases, and their prevalence in women are more than men. These disorders appear in a silent state and progress to advance stage before medical diagnosis (2).Toxic nodular goiter is the presence of thyrotoxicosis and thyroid nodules. It is prevalent in people more than 4o years old that have iodine deficiency. Incidence of this disease is much higher in European countries in comparison with Canada and United states, this belong to low quantity of consume dosage of iodine in European than Americans (3).

Hyperthyroidism or thyrotoxicosis manifests itself in production excessive amount of T3 and T4 hormones resulted in accelerated metabolic rate of tissues (4). Toxic multinodular goiter is a common cause of hyperthyroidism in which there is excess production of thyroid hormones thyroid from functionally autonomous thyroid nodules, which do not require stimulation from thyroid stimulating hormone (5) .

Hyperthyroidism resulted from several causes such as benign or malignant tumors, pituitary disturbance and autoimmune diseases (6). The pathogenicity of thyrotoxicosis progress through increasing activity and

hypertrophy of thyroid for long time, and then lead to develop of nodules. The origin of goiter is developed from consequence of hyperplasia of thyroid tissues (7).

Materials and Methods:

A. Materials:

1. Subjects of Study:

This study was carried out in the histopathology department of Hilla- Teaching Hospital over 5 months period. This study included 15 patients of both sexes, males and females and their ages ranged between 20-64 years old. Patients were admitted to hospital for surgical operation (Thyroidectomy) by consultant surgeons. Before surgical operation, blood samples were drowning from patients to perform hormonal analysis. Blood samples were also drowning from healthy subjects for comparison results.

B. Methods:

1. Determination of thyroid stimulating hormone (TSH), Triiodothyronine (T3) and Tetraiodothyronine (T4):

Thus method was performed by using Minividas method with kit supplied by Merieux Company, France.

2. Estimation of total serum protein: Biuret method was used for estimation of total serum protein of thyroid patients were according to Bishops *et al*, (8) .IgG detection was done by single radial immune diffusion (SRID Mancini method) (9).

2. Preparation of histological sections:

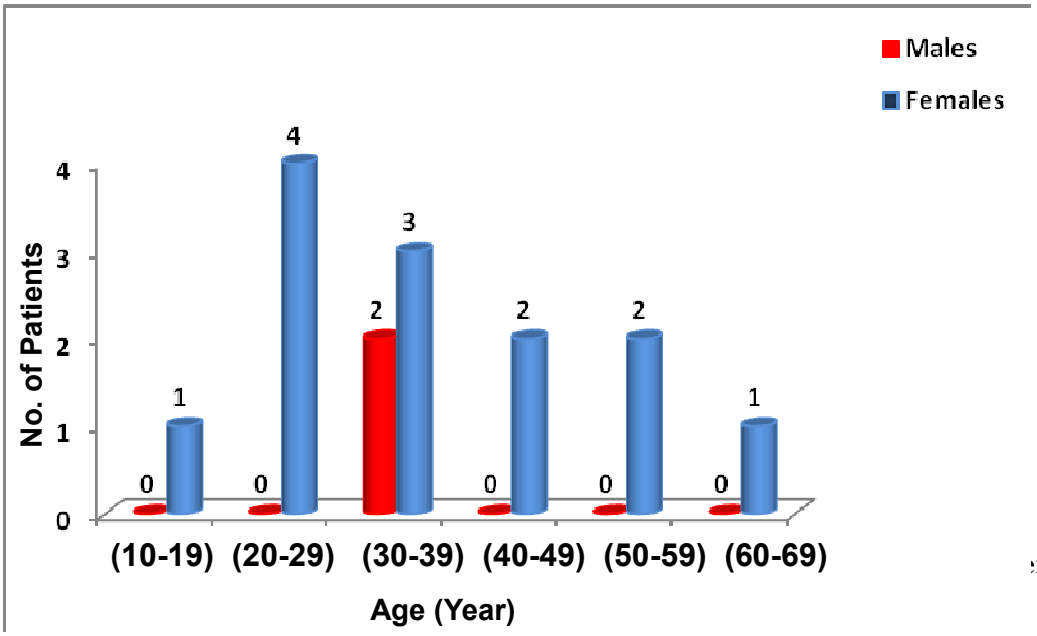
In this method, several steps were conducted such as color, number of nodules, cysts, calcifications and hemorrhage of thyroid tissues after thyroidectomy. All routine steps were performed to prepare histological sections which involved fixation, washing and dehydration, clearing, infiltration, embedding, sectioning and staining. By using Olympic microscope and ocular microscope, different histological changes of thyroid tissues were recorded (10).

3. Statistical analysis:

The statistical program was used to perform analysis of results Using two way analysis of variance (ANOVA) followed by application of lowest significant differences test at $P<0.05$ to confirm the statistical significances among studied groups (11).

Results:

Nodular toxic goiter presents in both sex but female appear to be more susceptible to this disease 13 of 15 with a rate % while only 2 male of 15 with a rate % . The age period 30-39 years show highest rate of infection (33.3 %) (figure 1) .



Thyroid hormones values show enhancement in all patients . TSH appear high in female than male with highly significant difference , T4 value show significantly increased in patients in comparison with healthy individuals (table 1).

Table (1): Means of TSH, T3 and T4 levels of patients affected with toxic nodular goiter.

Hormones levels	Males		Females	
	Control	Patients	Control	Patients
TSH(Miu/ml)	0.30±1.57*	0.07±0.85*	0.53±1.85*	0.24±2.80*
$T3_{(nmol)/L}$	0.19±1.28*	0.2±2.16*	0.14±1.59*	0.50±1.07*
T4(nmol/L)	2.05±71.12*	1.63±139.75*	3.71±74.59*	2.25±138.95*

- Values are means ± SD.

- Values with (*) are significantly at ($P<0.05$).

Total serum protein reveals decrease in nodular toxic goiter patients compared with control group (healthy persons). Serum protein concentrations show significantly decrease in all age groups , the lowest concentration reach 2.13 mg /dl . Total immunoglobulin type G concentration show significantly increase in serum of nodular toxic thyroid patients in compared with healthy individuals (table 2) .

Table 2. Serum IgG and total protein concentration of nodular thyroid patients .

Serum component Conc.	Nodular thyroid patients	Healthy
IgG mg /dl(M±SD)	1622.42±226.31	1124±187.34
Total protein mg/dl (M± SD)	2.04±1.06	4.76±1.12

Thyroid gland of nodular toxic goiter patients show variations in size , the size less than 100 cm form the highest number of patients , while the size 300-400 cm form the lowest number of patients (table 3).

Table 3. Distribution of patients affected with nodular toxic goiter according to size of thyroid gland.

Volume (cm)	Males	Females	Total No.	Percentage (%)
100-0 cm	1	6	7	46.67
200-100 cm	1	4	5	33.3
300-200 cm	0	2	2	13.3
400-300 cm	0	1	1	6.67
Total	2	13	15	100

Goiter patients show different number of nodules. Only one case show single nodule with a rate 6.6 % , while most patients 14 (93.3 %) reveals more than one nodules (table 4) .

Table 4. Distribution of patients affected with nodular toxic goiter according to the number of nodules .

No. of nodules	Males	Females	Total No	Percentage (%)
Single nodule	0	1	1	6.6
Multiple nodules	2	12	14	93.3
Total	2	13	15	100

Dissection of thyroid gland reveals present or absent of cyst , the number of cysts also differs . sixty percent of patients show no cysts , 33% show single cyst while 6.6 % reveals more than one cyst (table 5).

Table 5 . Distribution of goiter patient according to the number of cysts present in thyroid gland.

No. of cysts	Males	Females	Total No	percentage (%)
No cyst	1	8	9	60
Single cyst	1	4	5	33.3
Multiple cysts	0	1	1	6.6
Total	2	13	15	100

Gross examination of thyroid glands show variation in gland texture . Few patient 2 (13.3 %) glands reveals calcification while, others 13 (86.6%)with no calcification (table 6) .

Table 6 . Distribution of goiter patients according to texture of thyroid gland.

Calcifications	Males	Females	Total No.	percentage (%)
+ ve	0	2	2	13.3
– ve	2	11	13	86.6
Total	2	13	15	100

Dissecting of thyroid glands show hemorrhage in some glands 5 (33.3 %) , while all other glands 10 (66.6%) appear without hemorrhage (table 7) .

Table 7. Distribution of goiter patients according to presence of hemorrhage in thyroid gland.

Haemorrhage	Males	Females	Total No.	percentage (%)
+ ve	0	5	5	33.3
– ve	2	8	10	66.6
Total	2	13	15	100

Thyroid gland of goiter patients reveals various histology

ical changes . The main histological disorders is fibrosis that appear in 12 (80 %) of patients followed by hyperplastic nodules and lymphocytes infiltration (figure 2,3 and table 8) .

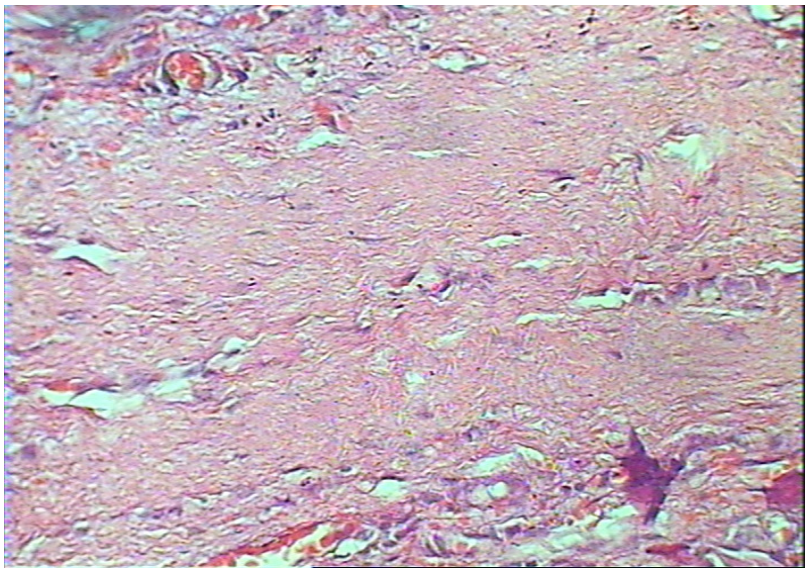


Figure 2. Cross section of patients goiter thyroid gland show nodular tissue fibrosis . H.E . 100x .

Table 8. Histological changes of thyroid affected with nodular toxic goiter.

Histological changes	Males	Females	Total No.	percentage (%)
Fibrosis	2	10	12	80
Calcification	1	4	5	33.3
Hyperplastic nodules	2	7	9	60
Lymphocytic infiltration	1	3	4	26.6
Vascular degeneration	0	1	1	6.6
Total	3	12	15	100

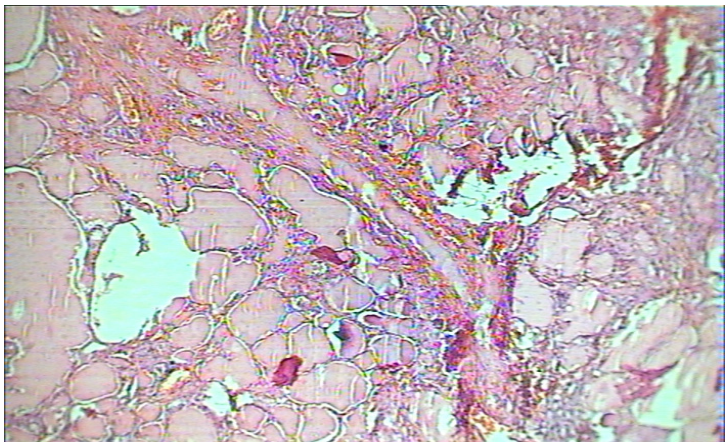


Figure 3. Cross section of patients goiter thyroid gland show tissue hyperplasia . H.E . 400x .

Histological examinations reported variations in measurements of thyroid components of patients in compared with normal tissues. Significant increase in epithelium thickness , colloid diameters and follicle diameter were noted in thyroid glands of patients (table 9) .

Table 9. Variation of follicles, colloid and epithelium diameter of thyroid affected with nodular toxic goiter.

Groups	Measurements		
	Thickness of epithelium	Diameter of colloid	Follicle
Normal tissue	0.005±0.57*	1.48±5.23*	1.10±5.89*
Pathological tissue	0.10±0.72*	1.38±8.98*	2.24±11.71*

- Values are means ± SD.

- Values with (*) are significantly at (P<0.05).

Discussion:

Results obtained from the present study indicated that the ratio of toxic nodular goiter (TNG) was 18.8% (15 patient) out of 80 patient affected with different thyroid diseases. These results were consistent with previous study (12). These previous studies confirmed that 20% of thyroid gland were affected with toxic goiter and suggested that acute iodine deficiency in diet or production of autoantibodies (IgG) against TSH receptors may be attributed to increase incidence of toxic goiter. Immunoglobulin's production enhanced after exposure of host to foreign agents , increase of their titer in this cases may be associated with hormonal disorders that correlated with presence of autoimmunity and immunodeficiency. There is a good correlation between the degree of lymphocytic infiltration of the thyroid gland and the titer of TPOAb. (13) .

Data of the present study pointed out that the number of affected women was 13 (66.6%) out of 80 patient, and the number of affected males was 2 (13.3%) out of 80 patient. From these results appear clearly that the women are more affected than males, and these results were agreed with previous studies (14), these studies suggested that hormonal imbalance at puberty and pregnancy is predisposing factor for occurrence of toxic goiter. These suggestion was supported by other studies (15) who confirmed that excess levels of estrogen hormone increase production of T3 and T4.

Levels of T3 and T4 hormones were significantly (P<0.05) higher than normal healthy subjects, these results were associated with significant decrease (P<0.05) in the levels of TSH of both sexes. Over production of T3 and T4 my attributed that S-cells produce autoantibodies which react with specific TSH receptors of thyroid. These antibodies activate follicular cells to produce excess amount of T3 anf T4 with reduction of TSH production by negative feedback mechanism (16).

Other researchers showed that there are nodules which consist of mononodular or multinodular originate from hypertrophy of some follicular cells and tend to produce excessive levels of T3 and T4 independently about TSH, the neighboring follicles becomes atrophy (17). Study of Lauberge *et al.*,(18) suggested that iodine deficiency in elderly may be implicated in the development of hyperthyroidism.

The gross appearance of thyroid histological sections confirmed that the ratio of thyroid glands which have volume more than 100 cm was 46.64, whereas thyroid glands which have volume more than 200 cm comprise 33.3%. These results were consistent with study of Gonezing *et al.,* (19). Concerning nodules, our results indicated that all affected gland have multi-nodular of benign form, and patient ages ranged between 20-70 years old. These data were consistent with previous studies (20).

The present results pointed out that the ratio of cysts was 40% out of the affected tissues, and 85% of these tissues were degenerative and necrotic. These results agree with previous study (21). Calcifications with hemorrhage were comprised 13.3% of affected tissues, and these calcifications caused the gland to become firm and more hard. Also, it had been found that there is accumulation of fibers associated with hemorrhage and comprise 33.3%. These data were consistent with previous study (22).

Concerning microscopical examinations of affected thyroid tissues showed that the affected thyroid with toxic goiter appear with bundles of fibers consist 80% out of affected tissues, these changes were also supported by Goudie *et al.,* (23).

The present study confirmed that 40% of glands showed several changes such as hyperplasia of follicles, variation of colloid volume, appearance of scallop. These data were agreed with previous study (22).

It also was appearance of lymphoid nodules with ratio 26%, degenerative blood vessels with ratio 6.6%. These changes originate from increase thyroid activity, cellular hypertrophy, cellular hyperplasia, increase number of follicles and nodules intern lead to compress the adjacent blood vessels and damage it (24).

Our study showed that the diameter of follicles, colloid, epithelium were significantly (P<0.05) taller than healthy tissues. These changes resulted from continuous stimulatory effected of more active and tend to have columnar shapes and increase their diameters and colloids (25).

In conclusion, histological changes of thyroid affected with toxic goiter may be result from increased activity of some follicles because of stimulatory effects of autoantibodies or hyperplasia of other follicles.

Conclusion: This study concluded that women are more susceptible to nodular thyroid than men. Furthermore, the enhancements of thyroid hormones and IgG titers pointed a significantly correlation between them. The study reveals also noticeable histopathological according to disease **.**

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