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Physiological Association of Thyroid Diseases with Thyroid Cancer Using Anti TG, Anti TPO, TSH, T4, T3

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Annotation: The thyroid gland is one of the main axes of the endocrine system, as it plays a vital role in regulating physiological processes through the secretion of hormones (Thyroxine - T4) and (Triiodothyronine - T3). This study aims to explore the physiological relationship between thyroid diseases and cancers using immune and hormonal indicators such as Anti-TG, Anti-TPO, TSH, T4 and T3. The research was conducted on 100 patients suffering from thyroid disorders, who were divided into two groups: a group of patients with thyroid cancer, and another group suffering from disorders without cancer. Using accurate analysis tools, immune and hormonal indicators were measured to explore the association between these indicators and the development of cancers. The results showed significant differences in some indicators such as TSH and Anti-TPO, indicating the importance of these indicators in early detection and diagnosis. The study also emphasized the importance of combining immune and hormonal indicators for a more comprehensive understanding of pathological mechanisms.

Keywords: Thyroid, Thyroid cancer, TSH, T4, T3, Anti-TPO, Anti-TG.

Introduction:

The thyroid gland is one of the most important endocrine glands in the human body, playing a pivotal role in regulating various vital processes. The gland produces the hormones thyroxine (T4) and triiodothyronine (T3), which control the metabolic rate and affect the functions of the heart,

blood vessels, and central nervous system [1][2]. Any imbalance in this gland can lead to serious health disorders ranging from hypothyroidism and hyperthyroidism to the development of cancerous tumors. Scientific research indicates that autoimmune diseases associated with the thyroid gland, such as autoimmune adenitis, may have a direct relationship with the development of thyroid cancers, as some studies show that antibodies such as Anti-Thyroglobulin (Anti-TG) and Anti-Thyroid Peroxidase (Anti-TPO) play a fundamental role in affecting the functions of the gland and contributing to tissue deterioration and the development of cancerous cells[4][3] .

Thyroid-stimulating hormone (TSH) levels show a clear association with the risk of thyroid cancer and studies show that high TSH levels stimulate cell division and abnormal growth of thyroid cells, increasing the risk of cancer development [5]. In addition, disturbances in T3 and T4 levels significantly affect the physiological environment of the gland, creating favorable conditions for the emergence of cancer cells. Accordingly, the combination of analysis of these hormonal and immunological indicators represents a scientific approach to better understanding the relationship between thyroid diseases and cancers.

Despite the progress in research on thyroid diseases and cancers, there is still a clear gap in studies that examine the physiological relationship between immune markers such as Anti-TG, Anti-TPO, and hormonal levels (TSH, T4, T3) on the one hand, and the risk of developing thyroid cancers on the other hand. Hence the importance of this research, which aims to bridge this gap by providing an integrated and data-based understanding. This study seeks to achieve a number of goals, most notably analyzing the relationship between immune and hormonal markers in patients with thyroid cancers compared to patients without it, in addition to providing scientific recommendations to improve early diagnosis methods.

The study includes a sample of 100 patients, divided into two groups: a group of patients with thyroid cancer, and another group of patients with thyroid disorders without cancer. The sample was carefully selected to ensure comprehensive scientific representation and achieve maximum accuracy in the results. The results of this research will contribute to guiding diagnostic and treatment strategies and improving the chances of preventing thyroid cancers, which represents a qualitative addition to the medical field .

Methods of work :

Blood serum and plasma samples were collected from 100 patients with thyroid disorders, where the sample included patients diagnosed with thyroid cancer and others with thyroid disorders without cancer. The samples were collected using standard tubes containing separator gel or anticoagulants such as Sodium Heparin and K3-EDTA. To ensure the safety of the samples, they were stored at a temperature ranging from 2-8 degrees Celsius for up to three days, or at a temperature of -20 degrees Celsius for a maximum of one month, taking care to avoid repeated freezing.

High-precision laboratory techniques were used to measure immune and hormonal indicators using three main devices. The first device is Elecsys Anti-Tg, which is based on the principle of competitive interaction to determine the levels of antibodies against Thyroglobulin (Anti-Tg) in serum. This device works by measuring the intensity of the chemical radiation resulting from the interaction between magnetic particles coated with Streptavidin and the samples, providing a measurement range of 10-4000 IU/mL. This device is accurate and effective in monitoring immune diseases and thyroid cancers. The second device used is Elecsys Anti-TPO, which aims to measure antibodies to the thyroid peroxidase enzyme (Anti-TPO).

This device also relies on the principle of competitive interaction, where antibodies in the sample compete with their counterparts labeled with Ruthenium (Ru) for binding sites in the enzyme. The device provides a measurement range of 5-600 IU/mL and is an important tool for the diagnosis of autoimmune diseases, including Hashimoto's Thyroiditis.

The third device, Elecsys TSH, was used to determine the concentration of thyroid stimulating

hormone (TSH) in serum and plasma samples. This device is based on the sandwich principle, where a ternary complex is formed that includes magnetic particles coated with streptavidin. The device is characterized by very high sensitivity, as it provides an accurate measurement range between 0.005-100 µIU/mL, making it an ideal tool for the early detection of thyroid disorders. After collecting the data, it was analyzed using specialized statistical programs, where the samples were divided into three main groups: the control group (control group), the group with low values, and the group with high values. The average values and standard deviation were calculated for each group, with analysis of variance tests performed to study the differences between groups. This methodology contributed to providing accurate results on the relationship between immune and hormonal indicators and thyroid disorders, which contributes to enhancing the understanding of the pathological mechanisms associated with thyroid cancers and improving diagnostic and treatment strategies.

Results :

The results of this study represent the cornerstone of understanding the physiological relationship between thyroid disorders and cancers, based on the analysis of immune and hormonal indicators. The data were carefully collected and classified into three main groups: the control group, the group with low values, and the group with high values, where hormonal indicators (T3, T4, (TSH) and immune indicators (Anti-TPO, Anti-TG) were studied. For each group, analyses were conducted using advanced devices to ensure the accuracy of the results and provide comprehensive insights into the role of these indicators in the development of thyroid diseases and cancers. These results highlight the significant differences between the groups and clarify the physiological links between the different values of these pathological indicators.

The following table (1) shows the distribution of T3 hormone values among the three groups. The table shows that T3 levels differ significantly among the groups, as the group with high values had the highest average values compared to the control group and the group with low values. This indicates the effective role of T3 hormone in metabolic processes associated with the development of thyroid cancers. A vertical chart will be attached here showing the variation of T3 levels among the three groups..

Table (1) T3 hormone levels (prepared by the researcher)

T3	Control	Low	High
Number of values T3	21	40	40
Minimum	0.6000	0.3000	0.7800
25% Percentile	0.9050	0.7150	1.298
Median	1.200	2.260	1.730
75% Percentile	2.055	2.968	2.360
Maximum	2.700	6.210	2.930
Mean	1.404	2.050	1.804
Std. Deviation	0.6503	1.351	0.6057
Std. Error of Mean	0.1419	0.2135	0.09577
Lower 95% CI	1.108	1.618	1.610
Upper 95% CI	1.700	2.482	1.997

Figure (1) shows the comparison of T3 hormone levels between three main groups: the control group, which represents normal values, the group with low values, and the group with high values. The figure shows using a box plot the distribution of statistical values for each group, where the center line inside the box reflects the median value, while the box borders represent the first percentile (25%) and the third percentile (75%), providing an understanding of the internal distribution of values. The vertical lines outside the box (Whiskers) represent the full range of values (from minimum to maximum). The figures above show the statistical values (p-values) between the different groups to assess significant differences, where the comparison between the

control group and the group with low values showed a significant difference (p=0.042), indicating that T3 levels in the group with low values differ significantly from the control group. On the other hand, comparisons between the high-value group and the control group (p=0.287) or between the high-value group and the low-value group (p=0.502) showed no significant differences, indicating a relative similarity in T3 levels between these groups. This analysis suggests that T3 levels may be more distinct at low levels compared to normal levels, while differences diminish as we move to high levels. These results support the use of T3 as a physiological marker for understanding thyroid-related disorders, especially when there is a significant decrease in values compared to normal values..

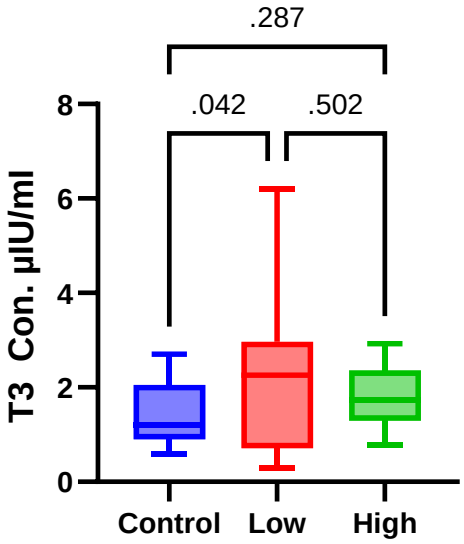

Figure (1) Distribution chart of T3 values among groups (prepared by the researcher)

Table (2) shows the distribution of T4 hormone values among the three groups. The data show that T4 levels in the group with high values significantly exceeded the average compared to the levels of the control group and the group with low values. The differences will be represented using a bar graph reflecting the minimum, average, and maximum values, which shows the relationship between the different groups.

Table (2) T4 hormone levels (prepared by the researcher)

T4	Control	Low	High
Number of values	21	40	40
Minimum	2.820	42.00	39.80
25% Percentile	117.0	92.25	81.08
Median	140.6	147.3	113.3
75% Percentile	174.9	193.0	184.4
Maximum	250.0	296.6	217.1
Mean	140.6	148.1	125.0
Std. Deviation	48.07	70.06	56.07
Std. Error of Mean	10.49	11.08	8.865
Lower 95% CI	118.8	125.7	107.0
Upper 95% CI	162.5	170.5	142.9

Figure (2) shows the distribution of T4 levels among three groups: the control group, the low-value group, and the high-value group. The data show slight variations between the groups, as the mean in the low group appears to be slightly higher than the control and high groups, however the differences between the groups are not statistically significant, as shown by the p values between

control and low p=0.605, between low and high p=0.892, and between control and high p=0.209. These results indicate that T4 is not a statistically significant differentiating factor between the three groups in this context, which may require a joint analysis with other indicators to understand its role more precisely. Table (2) and Figure (2) indicate that T4 hormone levels show slight variations between the three groups (control, low, high), as the group with high values recorded a higher mean compared to the control and low groups. However, these differences are not statistically significant according to the (p) values, indicating that T4 may not be a clear differential factor in determining pathological conditions associated with thyroid cancers or disorders. It may be necessary to conduct additional analysis to link the levels of this hormone with other indicators such as T3 or Anti-TG to obtain a more accurate understanding of its role in the development of pathological conditions.

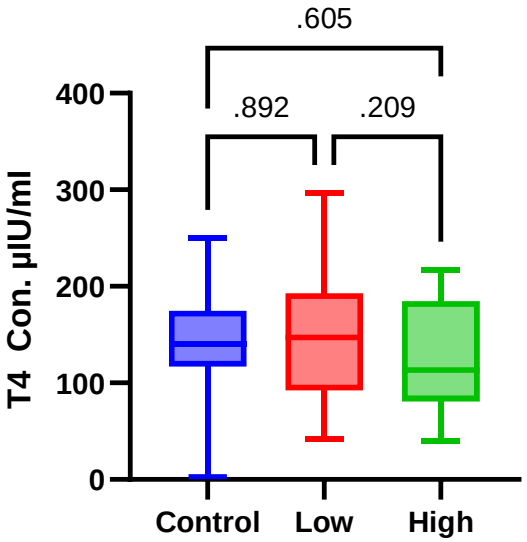

Figure (2) A chart showing the distribution of T4 values among the groups (prepared by the researcher)

Table (3) reflects the TSH measurements across the three groups. The data show that the group with the highest values had significantly higher TSH levels, indicating the effect of this hormone in stimulating thyroid cell activity and tumor growth..

Table (3) TSH hormone levels (prepared by the researcher)

TSH	Control	Low	High
Number of values	21	40	40
Minimum	1.170	0.005000	0.1000
25% Percentile	1.710	0.05000	0.6833
Median	1.930	0.1700	6.700
75% Percentile	2.650	5.700	20.15
Maximum	3.610	10.60	87.90
Mean	2.175	2.477	15.42
Std. Deviation	0.6811	3.143	20.58
Std. Error of Mean	0.1486	0.4970	3.254
Lower 95% CI	1.865	1.472	8.841
Upper 95% CI	2.485	3.482	22.00

The figure 3 shows the distribution of TSH values among three main groups, where the figure 3 indicates the presence of clear variations in TSH levels between groups, the control group shows

the lowest level with relatively low and limited values within a narrow range, the group with low values recorded levels almost similar to the control group, with no significant difference between them (p=0.996) In contrast, the group with high values shows a significant increase in TSH levels, with a wide variation in values and a clear upward deviation, the difference between the high group and both the control group and the low group is statistically significant (p<0.001), indicating the importance of TSH as a main indicator in these cases .

These results support the hypothesis that high TSH levels are closely related to physiological and pathological changes in the thyroid gland, especially in cases that show hyperactivity or major disorders, making it a sensitive indicator for evaluating these cases.

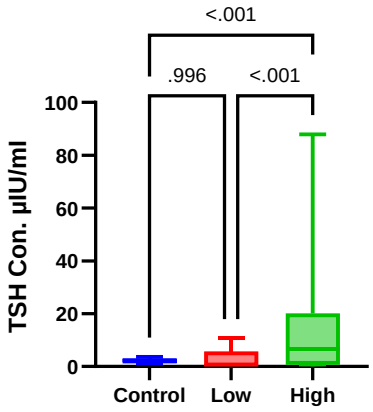

Figure (3) A chart showing the distribution of TSH values among the groups (prepared by the researcher)

The table 4 shows the statistical values of anti-TPO antibodies, which are an important indicator for the diagnosis of autoimmune diseases. The results showed a significant increase in the group with high values compared to the other two groups, reflecting the association of Anti-TPO with the development of autoimmune thyroid diseases and cancers..

Table (4) Anti-TPO levels (prepared by the researcher)

Anti TPO	Control	Low	High
Number of values	21	40	40
Minimum	7.000	6.800	8.100
25% Percentile	9.400	10.20	14.20
Median	11.10	16.90	69.60
75% Percentile	14.90	30.03	248.1
Maximum	343.2	192.6	600.0
Mean	35.34	37.48	169.1
Std. Deviation	78.92	50.23	197.9
Std. Error of Mean	17.22	7.942	31.29
Lower 95% CI	-0.5879	21.41	105.8
Upper 95% CI	71.26	53.54	232.4

Figure (4) shows the distribution of Anti-TPO levels among three groups: the control group, the low-value group, and the high-value group [7]. It appears that the control group and the low-value group had similar and statistically insignificant levels (p=0.998), while the high-value group recorded a significant increase in Anti-TPO levels, with significant differences compared to both the control group and the low-value group (p<0.001). This indicates that Anti-TPO plays a major role in the immune changes associated with thyroid diseases, especially in cases associated with a ..significant increase in this immune index

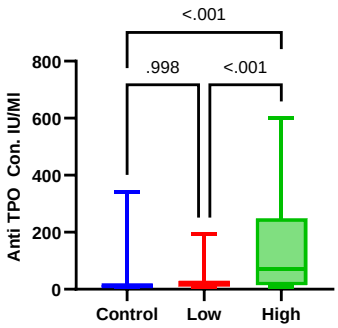

Figure (4) A chart showing the distribution of Anti-TPO values among groups. Prepared by the researcher

Table (5) reflects the results of measuring Anti-TG, where the group with high values showed a significant increase in the levels of this immune indicator. These results support the hypothesis that high Anti-TG is associated with an increased risk of thyroid cancer.

Table (5) Anti-TG levels (prepared by the researcher)

Anti TG	Control	Low	High
Number of values	21	40	40
Minimum	13.00	12.80	12.50
25% Percentile	13.25	14.23	20.05
Median	13.90	16.05	64.55
75% Percentile	21.95	49.63	295.2
Maximum	388.2	1054	4000
Mean	44.47	79.81	516.8
Std. Deviation	87.80	203.5	1189
Std. Error of Mean	19.16	32.17	188.0
Lower 95% CI	4.500	14.74	136.5
Upper 95% CI	84.43	144.9	897.1

Figure (5) shows the distribution of Anti-TG levels among three groups: the control group, the low-value group, and the high-value group. It appears that the Anti-TG levels in the control group and the low-value group are very close with no significant difference between them (p=0.984). However, the high-value group records a significant increase in Anti-TG levels compared to the other two groups, with a statistically significant difference compared to the low group (p=0.032), while the difference with the control group is not significant (p=0.061). These results indicate the role of Anti-TG as a potential factor in monitoring and evaluating immune conditions associated with thyroid diseases, especially when its levels are significantly elevated [8].

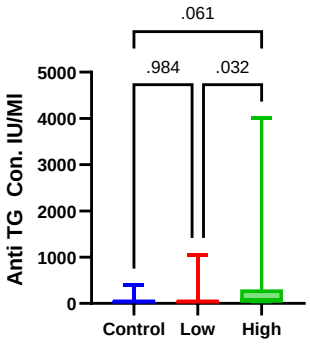

Figure (5) A chart showing the distribution of Anti-TG values among groups (prepared by the researcher)

Discussion :

This study provides important insights into the relationship between hormonal and immunological indicators and the development of thyroid cancer as the results showed that T3 levels were significantly higher in the high-value group compared to the control and low-value groups, with statistical significance between the control and low groups ($p=0.042$). This indicates the role of T3 in metabolic processes associated with the development of thyroid cancer. These results are consistent with the study which showed that T3 can affect cell growth in the thyroid gland, which reinforces its role as a physiological factor in the assessment of thyroid cancers [9].

For T4, the results did not show significant differences between groups, as the differences were slight and not statistically significant ($p>0.05$). This suggests that T4 may not be a decisive indicator in identifying thyroid cancer cases. This finding supports the findings of Andersen et al., 2003, who observed that T4 levels remain relatively stable in many thyroid conditions, highlighting the limitations of its role as a single diagnostic factor .

On the other hand, TSH levels showed a significant increase in the high-value group compared to the other groups, with significant differences ($p<0.001$). This supports the hypothesis that increased TSH may stimulate the growth of thyroid cancer cells. These results are consistent with Haymart et al., 2008, who found that high TSH is associated with an increased likelihood of extrathyroidal extension in cancer cases .

In addition, anti-TPO levels showed a significant increase in the high-value group compared to the control and low groups, with significant differences ($p<0.001$). This suggests the role of anti-TPO as an immunological marker in the diagnosis of autoimmune thyroid disorders, such as Hashimoto's thyroiditis and Graves' disease. These results are consistent with what was stated by (Gherghettaet al.,2017), who indicated that anti-thyroid peroxidase (Anti-TPO) antibodies are considered an important indicator in the diagnosis of autoimmune thyroid diseases .

As for anti-TG levels, they were significantly higher in the high-value group compared to the other groups, with statistical significance between the high and low groups ($p=0.032$). This suggests that anti-TG may be associated with an increased risk of thyroid cancer. These results are consistent with the study of (Lee et al., 2008), which showed that high anti-TG may be an indicator of an increased risk of papillary thyroid cancer in patients .

Conclusions :

The role of hormonal indicators :

- T3 showed clear differences between groups, as high levels were associated with an increased risk of thyroid cancer, reflecting its role as an important physiological indicator .
- T4 showed a relatively limited role in distinguishing between groups, as the differences between levels were not statistically significant .
- TSH showed very high levels in the high-value group, supporting its role as a major stimulator of abnormal thyroid cell activity .

Role of immune markers :

- Anti-TPO showed a close association with immune disorders leading to adenocarcinoma, with a significant increase in its levels in cancer cases compared to other groups .

Anti-TG showed a similar role to Anti-TPO, as high levels of it in the group with high values were associated with an increased risk of cancer, which strengthens the hypothesis of its association with cancer development .

Recommendations :

The study recommends that the analysis of immune and hormonal indicators such as T3, TSH, Anti-TPO, and Anti-TG should be combined to improve the accuracy of early diagnosis and

identify high-risk cases of thyroid cancer. Future research is also recommended to understand the precise physiological mechanisms of these indicators to develop more effective therapeutic strategies .

Conclusion :

This study indicates the importance of immune and hormonal indicators in understanding the nature of thyroid disorders and cancers. The results showed that indicators such as T3, TSH, Anti-TPO, and Anti-TG play key roles in distinguishing between different cases, which enhances their importance as diagnostic and therapeutic tools. The study also highlighted that the combination of immune and hormonal analysis can provide a deeper understanding of the pathological mechanisms associated with thyroid cancer .

Although some indicators such as T4 showed slight and insignificant variations, the combined role of these indicators when combined with other factors provides a more accurate framework for evaluation. The study demonstrates a close association between the pathophysiology of the gland and its cancers via these markers, which enhances the understanding of the pathological mechanisms and provides strong evidence for their role in diagnosis. This study also makes a valuable contribution to the field of thyroid research, highlighting the importance of future research focused on improving diagnostic strategies and developing therapies that target immune and hormonal mechanisms more effectively**..**

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