

Biochemical Study of Progranulin, ACE, and DPP4 in Hyperthyroidism Patients

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Abstract :

Background: Hyperthyroidism is characterized by a hypermetabolic state and elevated concentrations of thyroid hormones (T3 and T4), leading to multisystemic symptoms. Identifying novel biomarkers may enhance diagnosis and disease monitoring.

Objective: To investigate alterations in serum Progranulin, Angiotensin-Converting Enzyme (ACE), and Dipeptidyl Peptidase-4 (DPP-4) levels in hyperthyroidism patients and assess correlations with thyroid function parameters.

Methods: A case-control study included 90 blood samples divided equally between hyperthyroid patients and healthy controls. Thyroid hormones (TSH, T3, T4) were measured using a one-step sandwich enzyme immunoassay (VIDAS system), and Progranulin, ACE, and DPP-4 levels were quantified via ELISA. Statistical analysis was performed using SPSS v25, with significance set at $P \leq 0.05$.

Results: Hyperthyroid patients exhibited significantly elevated T3 and T4 ($P \leq 0.01$) and decreased TSH levels ($P \leq 0.01$) compared to controls. Serum Progranulin, ACE, and DPP-4 activities were significantly higher in patients ($P \leq 0.001$ for all markers). No significant differences were observed in relation to age and sex ($P \geq 0.05$).

Conclusion: Increased serum Progranulin, ACE, and DPP-4 levels in hyperthyroidism patients suggest their potential as auxiliary biomarkers for disease evaluation and monitoring.

Keywords: Hyperthyroidism, Progranulin, Angiotensin-Converting Enzyme, Dipeptidyl Peptidase-4, Biomarkers.

دراسة كيميائية حيوية للبروكرانولين وانزيم المحول للأنجوتنسين والداي ببيتايديل ببيتايديز4 لدى مرضى فرط نشاط الغدة الدرقية

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مستخلص:

يتميز فرط نشاط الغدة الدرقية بحالة فرط استقلابية وارتفاع في تراكيز هرمونات الغدة الدرقية (T3, T4)، مما يؤدي إلى ظهور أعراض متعددة تشمل عدة أجهزة في الجسم. وقد يُسهم تحديد مؤشرات حيوية جديدة في تعزيز دقة التشخيص ومراقبة تطور المرض. الكلمات المفتاحية: فرط نشاط الغدة الدرقية، داي ببيتايديل ببيتايديز 4 (DPP4)، الانزيم المحول للأنجوتنسين (ACE)، البراكرانولين (PRGN)، الكيمياء الحيوية السريرية، المؤشرات الحيوية.

Introduction

Thyroid dysfunction, particularly hyperthyroidism, affects the metabolic processes of multiple organ systems. The thyroid gland, situated anteriorly in the neck, secretes hormones that regulate basal metabolic rate and energy homeostasis. Hyperthyroidism, resulting from excessive secretion of triiodothyronine (T3) and thyroxine (T4), affects 1% of the global population and predominantly affects women aged 20–50 years.

The principal etiologies of hyperthyroidism include Graves' disease, toxic multinodular goiter, and thyroiditis. Among these, Graves' disease—an autoimmune condition—is the most prevalent cause. Conventional diagnostic strategies rely on thyroid function tests; however, recent studies suggest that additional biochemical markers may offer insights into disease mechanisms and severity.

Progranulin (PGRN) is a multifunctional growth factor involved in inflammation, wound repair, and immune regulation. Elevated serum PGRN levels have been observed in inflammatory and autoimmune diseases, suggesting a

potential role in the immunopathogenesis of hyperthyroidism.

Angiotensin-Converting Enzyme (ACE) plays a pivotal role in the renin-angiotensin system, regulating blood pressure and vascular function. Alterations in ACE activity have been implicated in various endocrine and cardiovascular disorders, but their association with thyroid dysfunction remains underexplored.

Dipeptidyl Peptidase-4 (DPP-4) is a serine protease involved in glucose metabolism, immune regulation, and inflammation. Changes in DPP-4 levels are documented in autoimmune and metabolic disorders, including diabetes mellitus and systemic lupus erythematosus.

Thus, this study aims to elucidate the alterations in serum Progranulin, ACE, and DPP-4 activities in hyperthyroid patients and investigate their potential as supplementary biomarkers for disease progression and management.

Materials and Methods

Study Design and Sample Collection: A total of 90 blood samples were collected between August 2022 and February 2024 at Kirkuk General Hospital. Participants were divided equally

into hyperthyroid patients and healthy controls based on clinical and laboratory evaluations.

Measurement of Thyroid Hormones: Levels of TSH, T3, and T4 were measured using a one-step sandwich enzyme immunoassay performed by the VIDAS automated analyzer (bioMérieux, France).

Determination of Progranulin, ACE, and DPP-4: Serum levels of Progranulin, ACE, and DPP-4 were quantified using ELISA kits (SunLong Biotech, China) following manufacturer instructions. Optical density (OD) was measured at 450 nm.

Statistical Analysis: Data were analyzed using SPSS version 25. Results were expressed as mean $\pm$ standard deviation (SD). Student's t-test was used to compare means between groups. A P-value ≤ 0.05 was considered statistically significant.

Results

Thyroid Hormone Levels: The results presented in Table 1 and Figure 1 show that the hyperthyroid group had significantly elevated T3 and T4 levels ($P < 0.01$) and reduced TSH levels ($P < 0.01$) compared to controls.

Table 1: Serum Levels of T3, T4, and TSH

Parameter	Control (mean $\pm$ SD)	Hyperthyroid (mean $\pm$ SD)	P-value
T3 (nmol/L)	1.49 $\pm$ 0.24	2.8 $\pm$ 0.4	$P < 0.01$
T4 (nmol/L)	90.78 $\pm$ 12.17	145.3 $\pm$ 14.5	$P < 0.01$
TSH (μ IU/mL)	2.3 $\pm$ 0.40	0.15 $\pm$ 0.03	$P < 0.01$

Figure 1: Serum Levels of T3, T4, and TSH

Progranulin Levels: The hyperthyroid group demonstrated significantly

elevated Progranulin levels compared to the control group ($P < 0.001$) (Table 2, Figure 2).

Table 2: Serum Progranulin Levels

Group	Progranulin (pg/mL, mean $\pm$ SD)	P-value
Control	10.90 $\pm$ 2.69	$P < 0.001$
Hyperthyroid	21.7 $\pm$ 5.1	

ACE Activity: ACE activity was significantly higher in hyperthyroid patients compared to controls ($P<0.01$) (Table 3, Figure 3).

Table 3: Serum ACE Activity (IU/L)

Group	ACE Activity (IU/L, mean $\pm$ SD)	P-value
Control	1.29 $\pm$ 0.27	$P<0.01$
Hyperthyroid	2.1 $\pm$ 0.29	

DPP-4 Activity: DPP-4 activity was significantly increased in hyperthyroid patients ($P<0.001$) (Table 4, Figure 4). No significant differences were found concerning age or sex ($P>0.05$).

Table 4: Serum DPP-4 Activity (IU/L)

Group	DPP-4 Activity (IU/L, mean $\pm$ SD)	P-value
Control	1.66 $\pm$ 0.27	$P<0.001$
Hyperthyroid	4.7 $\pm$ 1.09	

Discussion

The findings of this study confirm significant alterations in serum biomarkers among hyperthyroidism patients. Elevated T3 and T4 levels with suppressed TSH are consistent with typical hyperthyroid profiles.

The rise in Progranulin levels suggests heightened inflammatory or cellular stress responses associated with hyperthyroidism, particularly autoimmune etiologies like Graves' disease.

Increased ACE activity may reflect augmented renin-angiotensin system activation and vascular stress secondary to hyperthyroidism.

Enhanced DPP-4 activity correlates with immune dysregulation and altered glucose metabolism frequently observed in hyperthyroid patients.

Overall, these biomarkers could serve as valuable adjuncts for comprehensive assessment and monitoring of hyperthyroidism.

Conclusion

Hyperthyroidism is associated with significant elevations in serum Progranulin, ACE, and DPP-4 activities. These findings support the potential application of these markers in augmenting traditional thyroid function testing. Further studies are needed to explore their prognostic and diagnostic utility.

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