

## Evaluation of Brain Natriuretic Peptide levels In sera of Iraqi patients with hyperthyroidism and hypothyroidism.

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### Abstract

The thyroid gland is endocrine gland that is normally located in the lower front of the neck. Cardiovascular changes that accompany thyroid disorders could be stimulus for the release of BNP from heart ventricles.

Different factors, including stress environment conditions, have important role in pathogenesis of thyroid disorders and could possibly affect this response. Brain natriuretic peptide (BNP) is secreted from the ventricular myocardium in response to volume expansion and pressure overload. Serum BNP levels are also affected by thyroid function status, which was mostly related to a direct stimulatory effect of thyroid hormones on the secretion of BNP.

Serum levels of brain natriuretic peptide showed a highly significant increase in hyperthyroidism group compared with control group ( $p < 0.01$ ) and highly significant decrease in hypothyroidism group compared with control group. The results revealed a significant positive correlation between and T<sub>3</sub>, T<sub>4</sub> and BNP level in patients with hyperthyroidism while there was no significant correlation between the corresponding thyroid hormones and BNP level in patients with hypothyroidism.

**Key words:** Brain natriuretic peptide (BNP) and thyroid diseases.

تقييم مستويات الناتريوتريك الببتيد في مصل المرضى  
العراقين مع فرط وخمول نشاط الغدة الدرقية  
زينة عباس علي  
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**الخلاصة**

الغدة الدرقية هي غدة صماء تقع عادة في الجزء الأمامي السفلي من العنق. التغيرات في الاوعية القلبية التي تصاحب اضطرابات الغدة الدرقية يمكن أن يكون حافزا لإفراز عن BNP من البطينين في القلب. العوامل المختلفة، بما في ذلك ظروف البيئة والإجهاد، لها دور مهم في التسبب في اضطرابات الغدة الدرقية، ويمكن أن تؤثر ربما في هذا الرد. ويفرز الببتيد الناتريوتريك (BNP) من عضلة القلب البطيني ردا على توسيع الحجم والضغط الزائد.

وأظهرت مستويات المصل من الناتريوتريك الببتيد زيادة كبيرة للغاية في مجموعة فرط نشاط الغدة الدرقية مقارنة مع مجموعة التحكم (P > 0.01) وانخفاض كبير للغاية في مجموعة خمول الغدة الدرقية مقارنة مع مجموعة التحكم. أظهرت النتائج وجود علاقة إيجابية ذات دلالة إحصائية بين وT3، T4 ومستوى BNP في المرضى الذين يعانون من فرط نشاط الغدة الدرقية في حين لم يكن هناك ارتباط كبير بين المقابلة هرمونات الغدة الدرقية ومستوى BNP في المرضى الذين يعانون من خمول الغدة الدرقية.

**الكلمات المفتاحية:** الناتريوتريك ببتيد وامراض الغدة الدرقية.

**Introduction**

The thyroid gland is a butterfly-shaped endocrine gland that is normally located in the lower front of the neck. The thyroid's function is to synthesis thyroid hormones, which are secreted into the blood and then carried to every tissue in the body. Thyroid hormones help the body use energy, stay warm and keep the brain, heart, muscles, and other organs working as they should. Common thyroid dysfunctions, include hypothyroidism ,hyperthyroidism (e.g Grave's disease) ,Hashimoto's thyroiditis, goiter thyroid nodule and thyroid cancer[1].

Hyperthyroidism is the overproduction of thyroid hormones while hypothyroidism is defined as failure of the thyroid gland to produce sufficient thyroid hormone to meet the metabolic demands of the body. Untreated hypothyroidism can contribute to hypertension, dyslipidemia, infertility, cognitive impairment, and neuromuscular dysfunction[2].

Brain natriuretic peptide (BNP) is a cardiac neurohormone, composed of 32 amino acids, mainly secreted from the ventricles. Prohormone, pro brain natriuretic peptide (proBNP) is cleaved into the biologically active form BNP and amino terminal fragment of the prohormone NT-proBNP. Both peptides, BNP and NT-proBNP are present in the plasma[3]. The basic stimulus for the BNP secretion is increased ventricular wall tension in response to sodium and water retention, volume expansion and elevated end diastolic volume. It is well known that the synthesis and secretion of natriuretic peptides are under the complex control of neurohumoral and immune system. Increased BNP concentrations lead to reduction of blood pressure and plasma volume through coordinated action of the brain, adrenal glands, kidneys and blood vessels[4]. An increase of heart rate, total blood volume, left ventricular end-diastolic volume (LVEDV) and cardiac output in hyperthyroid state exerts the "stress" of the cardiac wall and could be possible stimuli for the secretion of BNP, and subsequently increased serum NTproBNP level [5].

Thyroid disease is quite common. Current estimates suggest that it affects as many as 9% to 15% of the adult female population and a smaller percentage of adult males. This gender-specific prevalence almost certainly results from the underlying autoimmune mechanism for the most common forms of thyroid disease, which include both Graves' and Hashimoto's disease. However, with advancing age, especially beyond the eighth decade of life, the incidence of disease in males rises to be equal to that of females[6].

The aim of the study is to find out the relationship between brain natriuretic peptide levels and thyroid hormones in Iraqi patients with hyperthyroidism and hypothyroidism. Previous studies found increased serum levels of BNP in both hyperthyroidism and hypothyroidism. No previous study elucidate the relationship between BNP, T3 and T4. In this study we tried to determine the relationship between BNP and thyroid hormones level in different cases of thyroid disorders.

## **Patients and Methods**

This study was conducted in Babylon Maternity and Pediatric Teaching Hospital and in the laboratory of Biochemistry Department, College of Medicine, University of Babylon. Serum brain natriuretic peptide was determined by using enzyme-linked immunosorbent assay (ELISA).

Full history was taken from all patients which include: age, residence, smoking, family history, medical history, drug history and surgical history. No drugs were prescribed to those patients that may interfere with the measured parameters. Thirty-six Iraqi patients with primary hyperthyroidism and primary hypothyroidism. Twenty-two subjects who are apparently healthy were enrolled in this study.

Twenty-two apparently healthy subjects (who are age and sex-matched with the patients group) were selected as a control group in the study. All control subjects have no history of chronic disease (as diabetes mellitus, hypertension, inflammatory disease such as rheumatoid arthritis) and not smoking. The statistical analysis was performed by using SPSS version 18 for windows. Data were expressed as Mean  $\pm$  SD. The normality of the distribution of all variables was assessed by the Student's F-test and Pearson correlation analysis that have been used to determine the significant difference between the two groups. P values less than 0.05 is considered significant.

## **Results and Discussion**

The results in (table- 1) reveals a highly significant increase in the sera level of BNP in patients with hyperthyroidism group cases compared with those of control group ( $P < 0.01$ ) and a highly significant decrease in the sera level of BNP in patients with hypothyroidism group cases compared with those of control group ( $P < 0.01$ ).

Hyperthyroidism and hypothyroidism induce significant changes in cardiac functions. The effects of hyperthyroidism on the heart include hemodynamic changes such as decreased systemic vascular resistance as well as increased cardiac output, heart rate, blood volume, blood pressure and impaired cardiac contractility. These changes result in ventricular stretch and pressure overload, which might cause concomitant rise in BNP concentrations. T<sub>3</sub> and T<sub>4</sub> stimulated release of BNP from both cultured atrial and ventricular myocytes in a dose-dependent manner [7].

An increase of heart rate, total blood volume, left ventricular end-diastolic volume (LVEDV) and cardiac output in hyperthyroid state exerts the “stress” of the cardiac wall and could be possible stimuli for the secretion of BNP, and subsequently levels increased of the serum BNP level [8].

Table (2) reveals a significant linear correlation between BNP and both T3 and T4 while there is no significant correlation between those parameters in patients with hypothyroidism. This can be attributed to the changes in the peripheral conversion of T4 to T3 in patients with hypothyroidism which may lead to changes in cardiac functions, hemodynamic factors which are induced by the concomitant increase of thyroid hormones while those changes were not significant in patients with primary hypothyroidism. Therefore the measurement of BNP is more important in patients with primary hyperthyroidism compared with the cases of hypothyroidism. Future studies are needed to further elucidate the effects of different treatment regimes of hyperthyroid patients on BNP levels of the corresponding patients[9].

**Table (1):- Biochemical parameters of hyperthyroidism and hypothyroidism and control Groups.**

<b>Parameter</b>	<b>hypothyroidism group n=18</b>	<b>Control group n=22</b>	<b>Hyperthyroidism Group n=18</b>
<b>BNP pg/ml Mean± SD Range</b>	<b>59.27±5.67 (40.1-59.2)</b>	<b>65.2±1.5 (62-66.9)</b>	<b>88.5±7.5 (70-99.5)</b>
<b>Total FT<sub>4</sub> µg/dl Mean± SD Range</b>	<b>2.05 ± 0.99 (0.56-3.399)</b>	<b>7.1 ±1.1 (4.47-9.05)</b>	<b>14.9 ±8.02 (1.48-24.5)</b>
<b>Total FT<sub>3</sub> ng/ml Mean± SD Range</b>	<b>0.41 ± 0.2 (0.11-0.70)</b>	<b>1.46 ±1.09 (0.96-7.67)</b>	<b>4.8 ±2.32 (1.40-8.10)</b>

Table (2): Pearson's correlation between BNP ,T3 and T4 levels in patients with hyperthyroidism

parameres		Hyperthyroidism		Hypothyroidism		
BNP	vs	T3	r	p	r	p
			<b>0.611</b>	<b>0.01</b>	<b>0.05</b>	<b>0.82</b>
BNP	vs	T4	<b>0.58</b>	<b>0.01</b>	<b>0.07</b>	<b>0.7</b>

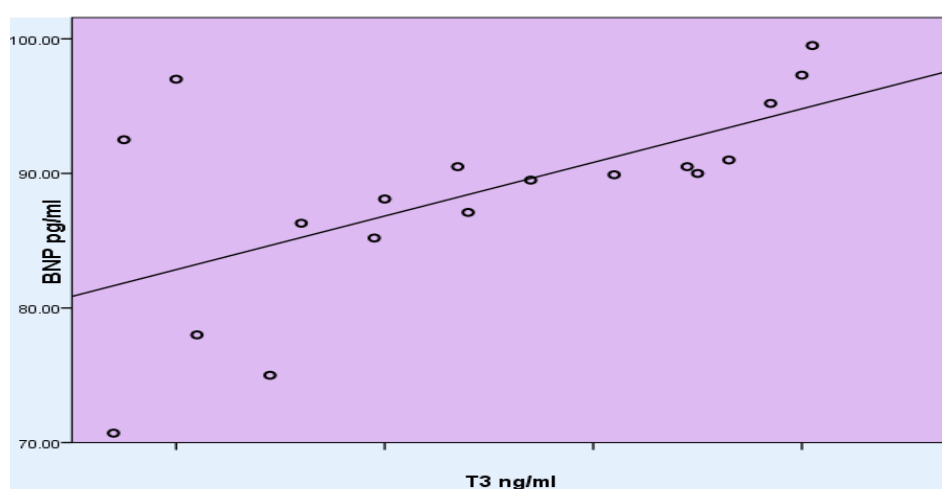


Figure (1):Correlation between T3 and BNP in patients with hyperthyroidism( $r=0.611$ ) ( $p<0.01$  ).

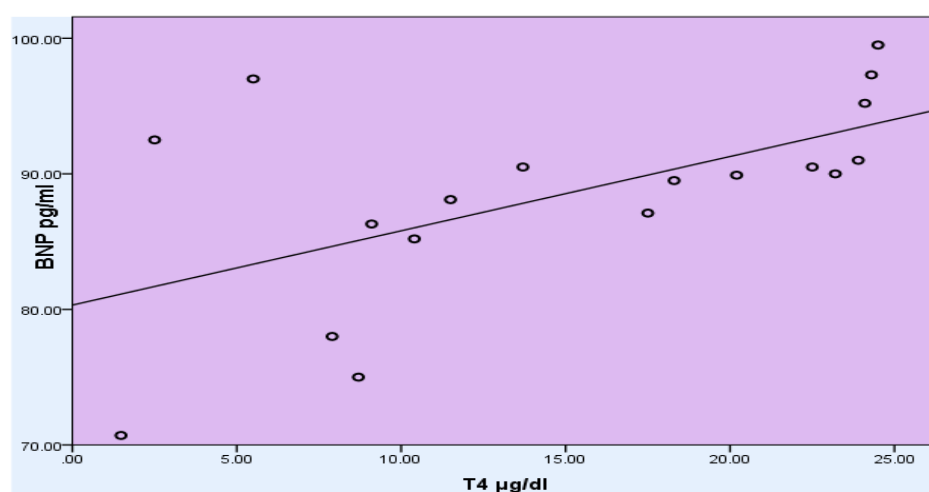


Figure (2):Correlation between T4 and BNP in patients with hyperthyroidism( $r=0.58$ ) ( $p<0.01$  ).

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