ORIGINAL RESEARCH PAPER

Volume - 12 | Issue - 07 | July - 2023 | PRINT ISSN No. 2277 - 8179 | DOI : 10.36106/ijsr

INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

SERUM LEVELS OF ADENOSINE DEAMINASE AND GAMMA GLUTAMYL TRANSFERASE IN HYPOTHYROID PATIENTS AND NORMAL INDIVIDUALS -A CASE CONTROL STUDY.

Clinical Biochemistry

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ABSTRACT

Background: Hypothyroidism is a clinical entity resulting from the deficiency of thyroid hormones or from their impaired activity. It is a common metabolic disorder in the general population. In India, 42 million peoples are suffering from thyroid diseases; hypothyroidism being the commonest thyroid disorder. Presently oxidative stress is considered as an important pathogenic mechanism in so many different diseases. **Objectives:** To evaluate and to compare the serum levels of Adenosine deaminase (ADA) and Gamma glutamyl transferase (GGT) in hypothyroid patients and normal individuals. **Methodology:** In this study we have taken a group of 50 clinically proven hypothyroid cases diagnosed by thyroid profile and an equal number of age and sex matched healthy subjects. After taking written informed consent the fasting venous blood sample was drawn from both the controls and cases for the assay of ADA and GGT by Enzymatic methods. **Results:** A significant increase in serum ADA and decrease in serum GGT was seen in hypothyroid patients compared to normal subjects. (p value < 0.001). **Conclusion:** The present study establishes ADA and GGT are useful biomarkers of oxidative stress in hypothyroidism.

KEYWORDS

Hypothyroidism, ADA, GGT.

INTRODUCTION:

Thyroid hormones are involved in the regulation of basal metabolic state and in oxidative metabolism.[1] Due to the changes in the number and activity of mitochondrial respiratory chain components by thyroid hormones will result in the increased generation of reactive oxygen species (ROS).[2,3] Oxidative stress is a general term used to describe a state of damage caused by ROS In so many different diseases oxidative stress is considered as an important pathogenic mechanism. The unbalancing between production of free radicals and antioxidant defences in the biological systems is known as oxidative stress.[4] There is an involvement of Thyroid hormones in the regulation of oxidative metabolism.[5]

Lipid peroxidation & damage to macromolecules & cellular structures of the organism, endothelium and erythrocytes may be caused by free radicals. It has been suggested that hypothyroidism leads to oxidative stress and to a reduction of antioxidant defenses. Under normal conditions; thyroid hormone will protect against oxidative stress which can be explained by the function of antioxidants as a defence system. The increased free radical production in the electron transport chain in the mitochondrial inner membrane and depletion of antioxidants is observed in hypothyroid individuals.[4]

There are several biochemical markers showing the extent of on-going oxidative stress in the body. Among them ADA and GGT as markers used to assess oxidative stress and antioxidant activity.

The deamination of adenosine to inosine in purine metabolism is catalysed by adenosine deaminase.[6] It is suggested to be an important enzyme for modulating the bioactivity of thyroid hormones.[7] A few prospective studies evaluated the oxidative stress variables and adenosine deaminase activity in patients with hypothyroidism.[8]

The primary role of cellular gamma glutamyl transferase is to metabolize extracellular reduced glutathione (GSH). Hypothyroidism associated ROS is the consequence of both increased production of free radicles and reduced capacity of antioxidants. In hypothyroidism there is increased levels of TSH might alter oxidative stress processes. Serum GGT activity might be an early and sensitive enzyme related to oxidative stress.[9]

Our objectives was to evaluate and to compare the serum levels of ADA and GGT, in hypothyroid patients and normal individuals and to establish the interrelation if any, between ADA and GGT, in patients with hypothyroidism.

MATERIAL AND METHODS

A case control study of serum ADA and GGT was carried out in patients with hypothyroid and controls. After obtaining institutional ethical clearance the study was carried out in clinically proven cases of hypothyroidism and age and sex matched healthy individuals as controls from medicine outpatient department of Subbaiah hospital attached to Subbaiah institute of medical sciences, Shimoga. A total number of 50 patients with hypothyroidism and an equal number of controls were selected based on inclusion and exclusion criteria for the present study. The patients and controls voluntarily participated in the study.

Inclusion criteria:

- Clinically proven cases of Hypothyroidism by thyroid profile with the age group of 30-70 years.
- An equal number of age and sex matched healthy individuals were included.

Exclusion criteria: Hypothyroid patients with

- Hepatic and renal disease
- Sepsis and severe inflammatory diseases
- Anaemia, hemochromatosis, Wilson's disease
- Diabetes mellitus
- Chronic alcoholism are excluded from the study.

Method of sample collection:

After taking written informed consent about 5 ml of venous blood was drawn under aseptic conditions in a sterile bulb from selected subjects after a period of overnight fasting of 10-12 hours. Serum was immediately separated by centrifugation and used for analysis. Serum ADA was estimated by PNP-XOD method and serum GGT by Szasz enzymatic method.

Statistical analysis:

Results were subjected for statistical analysis. Data thus obtained was expressed in terms of mean ± SD, proportions are analysed using independent student "t' test. p value ≤ 0.05 is considered as statistically significant.

RESULTS

Table 1: Comparison of thyroid profile, ADA and GGT in controls, subclinical hypothyroidism and hypothyroidism.

	Group -1 Control	Group-2 Subclinical Hypothyroidism	Group -3 Hypothyroidism	
Parameters	Mean ± SD	Mean ± SD	Mean ± SD	p*- Value, Sig

T3 (ng/dL)	2.02±0.44	1.6±0.29	0.9±0.2	p < 0.001 S
T4 (µg/dL)	8.4±1.8	6.9±1.6	2.9±0.9	p < 0.001 S
TSH (µIU/ml)	2.9±1.4	18.9±13.6	14.4±6.5	p < 0.001 S
ADA (U/L)	29.6±6.3	35.9±7.2	37.8±5.2	p < 0.001 S
GGT (U/L)	26.4±4.9	22.5±6	19±7.2	p < 0.001 S

Table 2: Post-Hoc tests:

	Groups	Tuckey HSD
T3	Control and Subclinical hypothyroidism	p- value <0.001
	Control and hypothyroidism	p- value <0.001
	Subclinical hypothyroidism and hypothyroidism	p- value <0.001
T4	Control and Subclinical hypothyroidism	p- value = 0.001
	Control and hypothyroidism	p- value <0.001
	Subclinical hypothyroidism and hypothyroidism	p- value <0.001
TSH	Control and Subclinical hypothyroidism	p- value <0.001
	Control and hypothyroidism	p- value <0.001
	Subclinical hypothyroidism and hypothyroidism	p- value= 0.261
ADA	Control and Subclinical hypothyroidism	p- value= 0.069
	Control and hypothyroidism	p- value <0.001
	Subclinical hypothyroidism and hypothyroidism	p- value <0.001
GGT	Control and Subclinical hypothyroidism	p- value= 0.061
	Control and hypothyroidism	p- value <0.001
	Subclinical hypothyroidism and hypothyroidism	p- value= 0.053

DISCUSSION:

Thyroid hormones are supposed to play an important part in the regulation of mitochondrial oxidative metabolism and antioxidant enzyme levels. Resh et al., found that hypothyroidism was associated with enhanced oxidative stress and lipid peroxidation.[10]

Table 1 shows one way ANOVA was performed to compare the effect of three groups (Control, Subclinical hypothyroidism and hypothyroidism).

Test shows that there is a statistically significant difference in mean values of T3, T4, TSH, ADA and GGT between at least two groups. [p-value <.001]

Post Hoc test using Tuckey's HSD test for multiple comparison found that there is a statistically significant difference in T3 and T4 between control and Subclinical hypothyroidism (p- value <.001), Control and hypothyroidism (p- value <.001) and Subclinical hypothyroidism and hypothyroidism (p- value <.001).

There is a statistically significant difference in TSH between control and Subclinical hypothyroidism (p- value <.001), Control and hypothyroidism (p- value <.001). There is no statistically significant difference in TSH between Subclinical hypothyroidism and hypothyroidism (p- value= 0.261).

In ADA between control and hypothyroidism (p- value <.001), subclinical hypothyroidism and hypothyroidism (p- value <.001) there is a statistical significance present. There is no statistically significant difference in ADA between control and subclinical hypothyroidism (p-value= 0.069).

Our finding is in accordance to the study done by Abbas et al.[11] Whereas the study done by Vishnu et al.,[12] shows that ADA level in hyperthyroid patients were within normal limit, which contradicts to our study.

Immunological disturbances of cell-mediated origin are believed to initiate from T-lymphocyte dysfunction. ADA plays a crucial role in lymphocyte proliferation and differentiation and shows its highest activity in T-lymphocytes.[13,14]

There is a statistically significant difference in GGT between control and hypothyroidism (p- value <.001. There is no statistically significant difference in GGT between control and hypothyroidism, subclinical hypothyroidism and hypothyroidism (p- value= 0.069). This is in accordance with Azizi et al.[15]

There is evidence that cellular GGT plays an important role in antioxidant defense systems.[16,17,18] This enzyme is widely distributed in the human body, especially in kidney and liver, and is frequently localized to the plasma membrane with its active site directed into the extracellular space.[19]

CONCLUSION:

As our findings suggests that there is increase in the serum levels of ADA and decreased levels of GGT in hypothyroid patients therefore its altered blood levels may help in predicting immunological dysfunction in thyroid disorders and might be one of the important biomarkers in predicting the disease.

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