



## EFFECT OF HYPOTHYROIDISM ON CREATINE KINASE AND LACTATE DEHYDROGENASE LEVEL

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### ABSTRACT

**Background:** Hypothyroidism is one of the most common causes of heart disease and there is known elevation in enzymes of thyroid disorder patients. We made this study to find out if CK and LDH activities were related to hypothyroidism and also using this enzymes as indicator to hypothyroidism, and to evaluate the relationship between CK, LDH and TSH levels. **Methodology:** In this study, thyroid function tests, serum CK and LDH activities were measured from adults newly diagnosed hyperthyroid (n=20) and hypothyroid patients (n=70) compared with healthy individual (n=50), at Almotacamil Medical Group(4), Khartoum, Sudan. **Results:** Elevation of CK activity was found in 7 patients (23%, 7/30) with subclinical hypothyroidism and in 4 patients (20%, 4/20) with overt hypothyroidism. The elevation of LDH activity was found in 14 patients (47%, 14/30) with subclinical hypothyroidism and in 6 patients (30%, 6/20) with overt hypothyroidism. In the hypothyroid patients, a positive correlation was found between CK activity and TSH ( $r = 0.381$ ,  $P = 0.006$ ). **Conclusion:** There were statistically significant elevations of CK and LDH activities, which can be used as parameters for screening hypothyroid patients.

**KEYWORDS:** Hyperthyroidism, hypothyroidism, lactate dehydrogenase, creatine kinase.

### INTRODUCTION

From 5-10% of individuals will be affected through the life period by endocrine disorders in case of overt abnormalities in thyroid function.<sup>[1]</sup> Thyroid stimulating hormone (TSH) and thyroid hormones (triiodothyronine, T3 and thyroxine, T4) in serum used for diagnosis and monitoring of therapy in thyroid disorder.<sup>[2]</sup> Overt thyroid disease has abnormalities in physiologic and biochemical measures<sup>[3]</sup>, which may be found in both subclinical hyperthyroidism and subclinical hypothyroidism and increase risk of illness with little abnormalities in thyroid function.<sup>[4,5]</sup> In subclinical hypothyroidism TSH concentration is elevated and free thyroid hormone levels (FT4 and FT3) at normal<sup>[6]</sup>, It has significant health implications more common than subclinical hyperthyroidism.<sup>[7]</sup> The prevalence of this condition is increasing with age and in women than men, reaching a peak over 74 years of age.<sup>[8,9]</sup>

The creatine kinase (CK) activity is a clinical marker for muscle damage and it is effected by physical activity, race, age and body mass.<sup>[10]</sup> Primary hypothyroidism patients have the acceptability for the increase concentrations of CK.<sup>[11]</sup> Some studies in thyroid disorder investigated CK<sup>[12]</sup> and lactate dehydrogenase (LDH) activities.<sup>[13]</sup> The goals of this study are focused

on the activities of CK and LDH in subclinical and overt hypothyroidism, subclinical and overt hyperthyroidism, and healthy persons; for the evaluation of (TT4 and TSH) levels and (CK and LDH) activities in thyroid disorders.

### MATERIALS AND METHODS

This is a case control study, which was performed on adults newly diagnosed thyroid dysfunction and healthy persons who agreed on verbal consent.

Patients having risk factors of increasing CK activities were not included in this study: intramuscular injection, surgery, stroke, excessive physical exercise, intoxication, seizure, certain medications (lithium, phenothiazines, statins and steroids), thyroidectomy and antithyroid medications. In this study we included 30 patients (24 females, 6 males) with subclinical hypothyroidism; 20 patients (15 females, 5 male) with overt hypothyroidism; 20 patients (16 females, 4 males) with hyperthyroidism; and 50 controls (healthy persons; 40 females and 10 males). In all subjects we measured serum CK and LDH activities using spectrophotometric device (BioSystem); and serum measuring TT4 and TSH levels by using enzyme immunoassay, at Almotacamil Medical Group(4), Khartoum, Sudan.

The patients were classified as follows: (1) subclinical hypothyroidism classified as TSH level more than 7.0 uIU/mL with a normal TT4 concentration; (2) overt hypothyroidism was defined as TSH level more than 7.0 uIU/mL with a TT4 concentration below normal; (3) overt hyperthyroidism defined as TSH level less than 0.40 uIU/mL (normal, 0.4 – 7.0 uIU/L) with an elevated TT4 concentration (normal, 5 – 13 ug/dL); and (4) subclinical hyperthyroidism defined as a TSH level less than 0.40 uIU/mL with a normal TT4 concentration.

One-Way ANOVA and Correlate were used in this study ( $P$ -value < 0.05).

## RESULTS

Elevation of CK activity was found in 7 patients (23%, 7/30) with subclinical hypothyroidism and in 4 patients (20%, 4/20) with overt hypothyroidism; keeping in mind the means of subclinical hypothyroidism, overt hypothyroidism, subclinical hyperthyroidism and overt hyperthyroidism were (130±52, 150±65, 115±30, 108±20) respectively [Table 1 and 2].

Elevation of LDH activity was found in 14 patients (47%, 14/30) with subclinical hypothyroidism and in 6 patients (30%, 6/20) with overt hypothyroidism; keeping in mind the means of subclinical hypothyroidism, overt hypothyroidism, subclinical hyperthyroidism, and overt hyperthyroidism were (457±189, 396±175, 285±63, 303±61) respectively [Table 1 and 2].

In hypothyroidism patients positive correlation was found between CK activity and TSH levels ( $r = 0.376$ ,  $p=0.007$ ), and no correlation between TSH and LDH ( $p=0.630$ ), and between LDH and CK (0.849), but in comparing subclinical hypothyroidism and overt hypothyroidism with control there were significant statistical differences in CK ( $p=0.011$ ,  $P=0.000$ ) and LDH ( $P=0.000$ ,  $P=0.000$ ) activities respectively [Table 1].

In hyperthyroidism patients correlation was not noticed between TSH and CK ( $P=0.285$ ), CK and LDH ( $P=0.266$ ) and TSH and LDH ( $P=0.737$ ). There was a strong correlation between TSH and TT4 ( $P=0.00$ ,  $r=0.821$ ). In comparing subclinical hyperthyroidism and overt hyperthyroidism with control there were no differences in CK ( $p=0.494$ ,  $P=0.835$ ) and LDH ( $P=0.572$ ,  $P=0.315$ ) activities respectively [Table 2], but there was difference in TT4 ( $P=0.010$ ,  $P=0.000$ ).

From the following tables there were differences in activities of CK between hyperthyroidism, hypothyroidism patients and controls.

**Table 1: Comparison of TT4, TSH, CK, and LDH levels between controls, overt and subclinical hypothyroid patients.**

Variables	Subclinical (n=30)	Overt (n=20)	P value
TSH	12.9±3.4	13±1.7	0.384
TT4	7.4±1.5	3.1±1	0.000
CK	130±52	150±65	0.129
LDH	457±189	396±175	0.092
	Subclinical (n=30)	Control (n=50)	
TSH	12.9±3.4	2.1±1.3	0.000
TT4	7.4±1.5	8±1.7	0.195
CK	130±52	106±21	0.011
LDH	457±189	260±43	0.000
	Overt (n=20)	Control (n=50)	
TSH	13±1.7	2.1±1.3	0.000
TT4	3.1±1	8±1.7	0.000
CK	150±65	106±21	0.000
LDH	396±175	260±43	0.000

TT4 = Total thyroxine; TSH = Thyroid stimulating hormone; and LDH = lactate dehydrogenase; CK = Creatine kinase.

**Table 2: Comparison of TT4, TSH, CK, and LDH levels between controls, overt and subclinical hyperthyroid patients**

Variables	Subclinical (n=10)	Overt (n=10)	P value
TSH	0.23±0.07	0.07±0.06	0.863
TT4	10.2±1.8	16.1±3.6	0.000
CK	115±30	108±20	0.712
LDH	285±63	303±61	0.733
	Subclinical (n=10)	Control (n=5)	
TSH	0.23±0.07	2.1±1.3	0.090
TT4	10.2±1.8	8±1.7	0.010
CK	115±30	106±21	0.494
LDH	285±63	260±43	0.572
	Overt (n=10)	Control (n=5)	
TSH	0.07±0.06	2.1±1.3	0.050
TT4	16.1±3.6	8±1.7	0.000
CK	108±20	106±21	0.835
LDH	303±61	260±43	0.315

TT4 = Total thyroxine; TSH = Thyroid stimulating hormone; and LDH = lactate dehydrogenase; CK = Creatine kinase.

## DISCUSSION

Results of the study showed an increase in CK activity in hypothyroidism with more increase in overt hypothyroidism than subclinical hypothyroidism patients and fairly equal in hyperthyroidism patients to controls with higher increase in subclinical hyperthyroidism than overt hyperthyroidism patients. CK activity correlated with TSH level in hypothyroidism and hyperthyroidism patients. These Results are confirmed with previous studies such as: Soufir *et al.*<sup>[14]</sup> and Beyer *et al.*<sup>[15]</sup> The

increase of CK activity in hyperthyroidism patients when compared with controls was contradicted with one other study.<sup>[16]</sup>

Elevated activity of CK by leakage of CK from cells by increased permeability of cell due to alteration in sarcolemmal membranes,<sup>[17,18]</sup> reduced turnover of CK because of hypothyroidism<sup>[19]</sup>, or leakage of the enzyme from muscle cells in primary hypothyroidism<sup>[20]</sup> with subnormal body temperature<sup>[19]</sup> accompanied with histological changes in muscle cells<sup>[21]</sup> and some of it has marked myopathy.<sup>[22]</sup>

In hypothyroidism patients pituitary gland releases TSH to increase levels of thyroid hormones and muscles may release CK into the blood as response to it.<sup>[15]</sup>

Elevation of CK in hypothyroidism patients often related to increase CK-MM isoenzyme<sup>[23]</sup> is produced by skeletal muscle.<sup>[24]</sup>

Results of the study showed an increase in LDH activity in hypothyroidism with more increase in subclinical hypothyroidism than overt hypothyroidism patients and decrease in hypothyroidism with more increase in overt hyperthyroidism than subclinical hypothyroidism patients.

Some studies found elevation of LDH in hypothyroidism patients<sup>[25,26]</sup> and other in primary hypothyroidism.<sup>[27]</sup>

When comparing LDH and CK activities in hypothyroidism patients and controls there were significant different between subclinical and controls ( $P=0.000$ ,  $P=0.011$ ) and the same between overt hypothyroidism and controls ( $P=0.000$ ,  $P=0.000$ ) respectively and not in hyperthyroidism.

LDH activity elevation may be from decrease clearance and/or increase release from the liver.<sup>[28]</sup>

#### Limitations

The study had some limitations such as small sample size, no correlation between body mass index, and no correlation at specific age.

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#### CONCLUSION

The study found that, whenever there was an increase in serum TSH levels, there will be a counter increase in serum CK activity in hypothyroidism patients. In hypothyroidism patients there were significant elevations in CK and LDH activities, so they can be used as parameters for screening of hypothyroidism patients and not for hyperthyroidism patients.

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