

Serum Levels of Muscle Enzymes in Hypothyroidism

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ABSTRACT

Introduction: Hypothyroidism is a common endocrine disorder in the general population in Bangladesh. The musculoskeletal involvement is significantly higher in hypothyroid patients admitted into the hospital. To the assessment of thyroid function tests which currently followed such as thyroid-stimulating hormone [TSH], tri-iodothyronine [T3] and thyroxine [T4] are not sometimes sufficient to clearly marking out the diagnosis of T3 and T4 levels. The present study was conducted to evaluate the role of an auxiliary biochemical parameter, creatine phosphokinase (CPK), aldolase in diagnosing hypothyroid disorders and to evaluate their prognostic value.

Objective: The key objective of the study was to evaluate the serum levels of muscle enzymes in hypothyroidism.

Materials and Methods: A total of 50 cases of hypothyroidism admitted into the department of medicine of Sir Salimullah Medical College & Mitford Hospital, Dhaka, Bangladesh was included in the study. The study period was April 2014 to August 2014. It was a prospective observational study. Purposive sampling was followed to collect the data. 3ml of the venous blood sample was drawn from the hypothyroid patients. Serum CPK estimation was carried out by colorimetric assay on Vitros250 (J&J) Dade Behring, CoulterAu480 Random Access Multi batch Chemistry Analyzer. Aldolases were measured by spectrophotometric determination by using the ultraviolet procedure. Thyroid hormones were measured by the chemiluminescence immunoassay method on the Beckman colter access 2 auto analyze system.

Results: The age of the patients with hypothyroidism ranged from 15-65 years. The mean age was 36.62±7.80 years. The highest numbers of patients were in the 30-45 years group. In hypothyroid cases female to male ratio was 4: 1. The

commonest general symptom of hypothyroid cases in the present study was weight gain (68%) followed by cold intolerance (54%), hoarseness of voice (44%), fatigue (42%), goiter (22%). Normal CPK level was 12% & incases of aldolase were 36%. Mean CPK level was 240.0±22.36, and aldolase 12.0±2.36, which is statistically significant (P<0.05) before starting thyroxin therapy.

Conclusion: According to this study hypothyroidism is common in the third & fourth decade of life. Female is more affected than the male. Since a significant number of patients with hypothyroidism present with myopathy, so it may conclude that CPK and aldolase measurements may be useful as an auxiliary diagnostic tool for the diagnosis of hypothyroid disorders, and it may also indicate as a helpful prognostic parameter.


Keyword: Hypothyroidism, Serum Level, Muscle Enzymes, Endocrine Disorder.

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INTRODUCTION

The thyroid is a common disease in Bangladesh. Hypothyroidism is a clinical term of thyroid disease causing a deficiency of thyroid hormones or from their impaired activity.¹ Hypothyroidism is a frequent metabolic disorder in the general population. Thyroid hormones perform a wide array of metabolic functions including regulation of lipid, carbohydrate, protein, electrolyte and mineral

metabolisms. Overt abnormalities in thyroid function are common endocrine disorders affecting 5-10% of individuals over a life span.² Clinical symptoms and signs are often nonspecific, and the diagnosis and monitoring of therapy depend crucially on measurements of thyroid hormones (T3 and T4), and thyroid-stimulating hormone (TSH) in blood. Hypothyroidism is associated

with an increase in the risk of many other diseases, as well as abnormalities in biochemical and physiological function.³⁻⁵ Hypothyroidism is increasingly being recognized as having significant health implications.⁶ The prevalence of this condition is higher in women than men and increases with age, reaching a peak of 21% in women and 16% in men over 74 years of age.^{7, 8} Musculoskeletal disorders, like muscle aches, weakness & stiffness often accompany thyroid dysfunction. In life-threatening cases it can cause rhabdomyolysis (acute muscle breakdown).⁸ Sometimes, the disease causes muscle enlargement along with muscle weakness. Hypothyroidism may also cause adhesive capsulitis, Dupuytren's contracture, trigger finger, limited joint mobility, and carpal tunnel syndrome. The muscle enzyme, creatine kinase (CK) and aldolase are important clinical markers for muscle damage in hypothyroidism.⁹ Their activity in healthy individuals depends on age, race, lean body mass and physical works.¹⁰ Concentrations of creatine phosphokinase (CPK) and aldolase in serum are often increased in patients with hypothyroidism.^{11,12} In recent years a very few studies have been conducted to establish a relationship of CK & aldolase activity in hypothyroid diseases.¹³ However, a correlation has been consistently described between muscle enzyme levels and circulating concentrations of T3, T4, or TSH,^{9,10,14} but sometimes they are not sufficient to clearly make out the diagnosis as T3 and T4 levels. In that case, as an alternative biochemical parameter, CPK and aldolase, may play an important role in diagnosing hypothyroid disorders and to evaluate their prognostic value.^{15,16} Musculoskeletal disorders often accompany thyroid dysfunction. The pathogenesis of these CK & aldolase elevation is not well understood but may be caused by a reversible defect in glycogenolysis, direct cell damage, and /or reduced metabolic clearance of CK with aldolase.¹⁷ Skeletal muscle is affected by hypothyroidism more profoundly in cases of overt hypothyroidism, less so in subclinical hypothyroidism.^{18,19} The assay of creatine kinase and aldolase activity in serum is extremely valuable in screening hypothyroidism and monitoring the treatment. The aims of this study are to determine the serum levels of CPK and aldolase in hypothyroidism, before and after thyroxin replacement therapy; and to evaluate the relationship between them. Limited studies are available in our country especially in the North area though the hypothyroid patient is more common here. With this background, this study is aimed to identify a relationship between the level of serum CPK & aldolase in a hypothyroid patient before and after thyroxin replacement therapy for proper management of the hypothyroid disorder.

MATERIALS AND METHODS

A total of 50 cases of hypothyroidism admitted into the department of medicine of Sir Salimullah Medical College & Mitford Hospital Dhaka, Bangladesh. It was a prospective observational study. Purposive sampling was followed for data collection. 3ml of the venous blood sample was drawn from the hypothyroid patients. Serum CPK estimation was carried out by colorimetric assay on Vitros 250 (J&J) Dade Behring Dimension RxL. Coulter Au480 random access multi-batch chemistry analyzer. Aldolases were measured by spectrophotometric determination by using the ultraviolet procedure. Thyroid hormones were measured by the chemiluminescence immunoassay method on Beckman Colter access 2 auto analyzers. A drop of patient sample is deposited on

the VITROS CK slide and is evenly distributed by the spreading layer to the underlying layers. When the sample is deposited on the slide, creatine kinase catalyzes the conversion of creatine phosphate and ADP to creatine and ATP. In the presence of glycerol kinase (GK), glycerol is phosphorylated to L- α -glycerophosphate by ATP. Oxidation of L- α -glycerophosphate to dihydroxyacetone phosphate and hydrogen peroxide occurs in the presence of L- α -glycerophosphate oxidase (α -GPO). Reflection densities are monitored during incubation. Aldolase catalyzes the splitting of D-fructose 1, 6-diphosphate into 2 molecules of triose phosphate, 1 of which is D-glyceraldehyde. The addition of triose phosphate isomerase converts the glyceraldehyde to dihydroxyacetone, which in turn is converted to alpha-glycerol phosphate by the further addition of alpha-glycerol phosphate dehydrogenase. This last enzymatic step also involves the conversion of NADH to NAD with a progressive loss of the characteristic absorbance of NADH at 340 nm. This conversion of NADH is measured kinetically. After completion of the collection of data in a pre-designed & structured questionnaire by interviewing and observing every case, tables were prepared by the observed values; mean and standard deviation were calculated. Levels of significance were tested by independent t-test and chi-square test. The statistical software SPSS 23.0 was used for the analysis of the data.

RESULTS

The age of the patients with hypothyroidism ranged from 15-65 years. The mean age was 36.62 ± 7.80 years. The highest number of patients was in the 30-45 years group. In hypothyroid cases female to male ratio was 4: 1. The commonest general symptom of hypothyroid cases in the present study was weight gain 68% followed by cold intolerance 54%, hoarseness of voice 44%, fatigue 42%, and goiter 22%. In the present study serum, CPK and aldolase levels in hypothyroid patients were markedly elevated, found among 84% and 60% of patients respectively at the time of diagnosis. Normal CPK level was 12% & increases of aldolase were 36%. Mean CPK level was 240.0 ± 22.36 , and aldolase 12.0 ± 2.36 , which is statistically significant ($P < 0.05$) before starting thyroxin therapy. After 6 weeks of standard thyroxin therapy, the resolution of CPK and aldolase level occurred. It became normal 92% of CPK 100.0 ± 19.36 , and 70% of aldolase 4.2 ± 2.2 , which is statistically significant ($P < 0.05$). The high degree of positive correlation was found between serum CPK & aldolase value before and after the treatment of hypothyroidism. Among the total patients, 8% were subclinical hypothyroid rest 92% were overt hypothyroidism. The most common causes of hypothyroidism were spontaneous atrophic hypothyroidism 33 patients (66%), followed by Hashimoto's thyroiditis 11 patients (22%), iatrogenic (post-surgery & post-radiation) 3 patients (6%) and graves' hypothyroidism 2 patients (4%), panhypopituitarism 1 patients (2%). The result of the study showed serum CPK and aldolase levels in hypothyroid patients were markedly elevated, found among 84% and 60% of patients respectively, at the time of diagnosis. Normal CPK level was 12% & increases of aldolase were 36%. Mean CPK level was 240.0 ± 22.36 , and aldolase 12.0 ± 2.36 , before starting thyroxin therapy. After 6 weeks of standard thyroxin therapy, the resolution of CPK and aldolase level fairly occurred. It became normal 92% of CPK 100.0 ± 19.36 , and 70% of aldolase 4.2 ± 2.2 which is statistically significant ($P < 0.05$). The

high degree of positive correlation was found between serum CPK & aldolase value before and after the treatment of hypothyroidism. Table-1 shows the gender wise distribution & ratio of the hypothyroid patients. Among total patient of 50, female preponderance was 40 (80%) than male 10 (20%). Ratio of male and female is 1: 4.

Table-2 shows age of the patients with hypothyroidism was ranged from 15-50 year. The mean age was 36.62±7.80 years. The highest number of patients was in the 30-45 age years group. Table 3 shows that among 50 patients; 33 patients are from rural area whereas 17 patients are from urban area. Out of 33 rural patients are 25 female and 8 are male. Among urban patients 15 are female and 2 are male.

Table-4 shown: The general symptom of hypothyroid cases in the present was found weight gain (68%) was most common followed by cold intolerance (54%), hoarseness of voice (44%), fatigue (42%), and finally goiter (22%)

Table-5 shown: Among total patients 50, subclinical hypothyroidism was 4(8%) and overt hypothyroidism was 46(92%).

Table 1: Gender ratio of the studied patients (N=50)

Gender	n	%
Male	10	20.0
Female	40	80.0
Base	50	100.0
Ratio	1 : 4	

Table 2: Age and gender wise distribution of patients (N=50)

Age	n	%	Male	Female
15 – 25 years	5	10.0	2	3
26 – 35 years	15	30.0	3	12
36 – 45 years	25	50.0	4	21
>45 years	5	10.0	1	4
Base	50	100.0	10	40
Mean ±SD = 36.62±7.80				

Table 3: Area wise distribution of patients (N=50)

Area	No of patient	Male	Female
Rural	33	8	25
Urban	17	2	15
Base	50	10	40

Table 4: Distribution of general symptoms of hypothyroid cases (N=50)

General Symptoms	Male (n-10) n (%)	Female (n -40) n (%)	Total Patients (n-50) n (%)
Cold intolerance	4 (40%)	23 (57.5%)	27 (54%)
Weight gain	7 (70%)	27 (67.5%)	34 (68%)
Hoarseness of voice	3 (30%)	19 (47.5%)	22 (44%)
Goiter	1 (10%)	10 (25%)	11 (22%)
Fatigue	4 (40%)	17 (42.5%)	21 (42%)

Table 5: Distribution of sub clinical hypothyroidism and overt hypothyroidism (N=50)

Subclinical hypothyroidism	Overt hypothyroidism	Total
Frequency (%)	Frequency (%)	N (%)
4(8%)	46(92%)	50(100%)

Table 6: Distribution of causes of hypothyroidism (N=50)

Causes of hypothyroidism	n	%
Spontaneous atrophic hypothyroidism	33	66.0
Hashimoto's thyroiditis	11	22.0
Graves' hypothyroidism	2	4.0
Pan hypopituitarism	1	2.0
Iatrogenic	3	6.0
Base	50	100.0

Table 7: Serum level of CPK diagnosis (N=50)

Serum CPK Level (U/L)	n	%	p-Value
>170	42	84.0	< .005
50-170	6	12.0	> .005
<50	2	4.0	> .005
Base	50	100.0	
Mean ±SD = 240 ± 22.36			

Table 8: Serum Aldolase level diagnosis (N=50)

Serum Aldolase Level (U/L)	n	%	p-Value
>8.1	30	60.0	< .005
1.5-8.1	18	36.0	> .005
< 1.5	2	4.0	> .005
Base	50	100.0	
Mean ±SD = 12± 2.36			

Table 9: Serum level of CPK after 6 weeks of standard thyroxin therapy (N=50)

Serum CPK Level (U/L)	n	%	p-Value
50-170	46	92.0	< .005
>170	3	6.0	> .005
<50	1	2.0	> .005
Base	50	100.0	
Mean ±SD = 100 ± 9.36			

Table 10: Serum level of Aldolase after 6 weeks of standard thyroxin therapy (N=50)

Serum Aldolase Level (U/L)	n	%	p-Value
1.5- 8.1	35	70.0	< .005
> 8.1	18	36.0	> .005
<1.5	2	4.0	> .005
Base	50	100.0	
Mean ±SD = 100 ± 9.36			

Table-6 shown: The most common causes of hypothyroidism were spontaneous atrophic hypothyroidism 33 (66%), followed by Hashimoto's thyroiditis 11(22%), iatrogenic 3 (6%), graves' hypothyroidism 2 (4%) and finally pan hypopituitarism 1 (2%).

Table-7 shown that, elevated serum CPK found among total patients 84% patients were more than normal, 12% were normal & below normal were 2%. Mean of CPK level 240.0±22.36 & P value <0.005 which was statistically significant.

Table- 8 shown that, elevated serum aldolase found among total patients 60% patients were more than normal, 36% were normal & below normal were 4%. Mean aldolase was level 12.0 ± 2.36 , P value < 0.005 which was statistically significant.

Table-9 shown that, resolution of serum CPK found among total patients 92% patients were normal, more than normal 6% & below normal 2%. Mean CPK level was 100.0 ± 9.36 , P value < 0.005 which was statistically significant.

Table 10 shown that, resolution of serum aldolase 70%, 36% more than normal & rest 4% patients were below normal. Mean aldolase level was 4.2 ± 2.2 , P-value < 0.005 which is statistically significant.

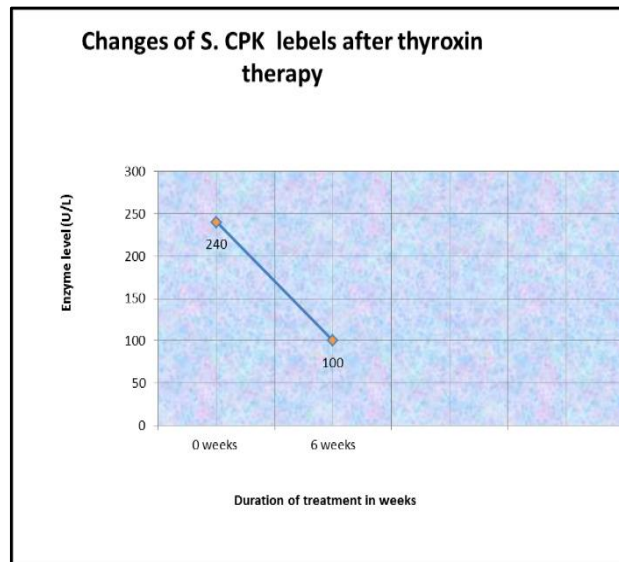


Figure 1: Resolution of serum CPK level in hypothyroid patients after 6 weeks of standard thyroxin therapy

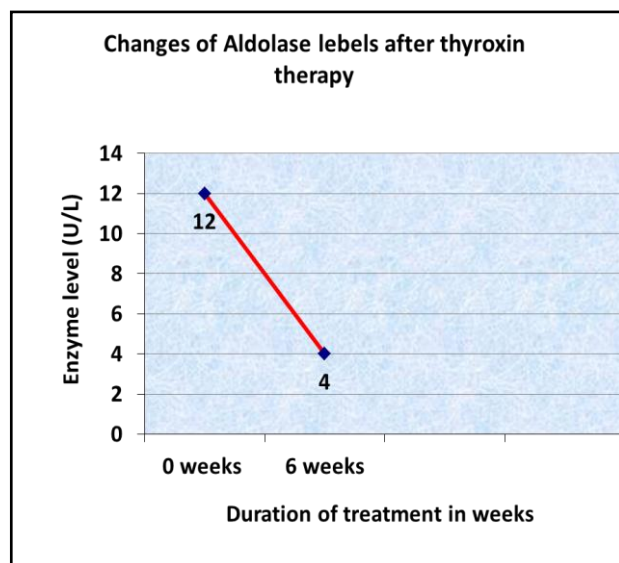


Figure 2: Resolution of serum Aldolase level in hypothyroid patients after 6 weeks of standard thyroxin therapy

DISCUSSION

Hypothyroidism is one of the most commonly occurring thyroid disorders worldwide. This study was focused to assess the involvement of muscles in hypothyroidism using biochemical markers of muscle damage such as serum creatine kinase (CK), aldolase and also to correlate the activity at diagnosis of

hypothyroidism and after 6 weeks of standard thyroxin therapy. Hypothyroidism is a very common condition for women than in men. In hypothyroid cases female to male ratio was 4:1.^{20,21} found that ratio 2.68 and 3.75 respectively. The commonest general symptom of hypothyroid cases in the present study was weight gain (68%) followed by cold intolerance (54%), hoarseness of voice (44%), fatigue (42%), goiter (22%). Vishwanath also found to be the commonest general symptom weight gain (65.44%) followed by cold intolerance 58.06%, hoarseness of voice 38.39%, fatigue 39.94% and goiter 21.80%.²¹

In the present study serum, CPK and aldolase levels in hypothyroid patients were markedly elevated, found among 84% and 60% of patients respectively at the time of diagnosis. Normal CPK level found 12% patient & normal aldolase was 36%. Mean CPK level was 240.0 ± 22.36 , and aldolase 12.0 ± 2.36 , which was statistically significant ($P < 0.05$) before starting thyroxin therapy. After 6 weeks of standard thyroxin therapy, the resolution of CPK and aldolase level occurred. It became normal 92% of CPK 100.0 ± 19.36 , and 70% of aldolase 4.2 ± 2.2 , which was statistically significant ($P < 0.05$) after thyroxin therapy. A high degree of positive correlation was found between serum CPK & aldolase value before and after the treatment of hypothyroidism. The correlation was found to be statistically significant ($P < 0.05$) in each case. A hospital-based descriptive study found CK elevation was observed in 57%–90% of patients with hypothyroidism.²² Another study shows that, the serum CPK fairly constant rate of fall with a half time for disappearance of approximately 10 to 12 days of thyroxin therapy in hypothyroid patients.²³ Whereas, we observed the result after six weeks of treatment. Another study shown, approximately 60% of the hypothyroid patient had elevated level of aldolase, whereas 90% had abnormal CPK activities, the majority level, between 100 and 300 units, some are much higher.¹⁹

CONCLUSION

A significant number of hypothyroid patients presents with myopathy, both CPK and aldolase are found elevated at diagnosis and fairly fall after six weeks of treatment, which is near to the results of previous studies. According to this study, hypothyroidism is common in the third & fourth decade of life. Female is more affected than the male. So it may conclude that CPK and aldolase measurements may be useful as an auxiliary diagnostic tool for the diagnosis of hypothyroid disorders, and it may also indicate as a helpful prognostic parameter. The significant elevation in serum CK and LDH activities indicates that these can be used as parameters for screening hypothyroid patients but not hyperthyroid patients. Gradually increasing hypothyroid patients are creating a burden on health care centers as well as in the community. The study is expected to enrich existing knowledge and capability as well as help future researchers in this field. The result of this study is expecting to be helpful for the convenient and successful management & treatment of hospitalized hypothyroid cases all over in Bangladesh.

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