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A Study of Creatine Kinase, Lactate Dehydrogenase Activity and Serum Creatinine in Diagnosed Case of Hypothyroidism and Control Subjects : A Case-Control Study

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Abstract

Background: Thyroid hormones regulate our body's metabolism and influence virtually every organ system in the body. hypothyroidism may be associated with a wide range of muscle disturbances varying from myalgia to a true myopathy. biochemical tests such as Creatine Kinase (CK) or Creatine phosphokinase (CPK) and Lactate Dehydrogenase (LDH) can be used. Of these, CK is the most sensitive indicator and measure of muscle damage and LDH is a general indicator of tissue damage. studied the serum creatine kinase in thyroid disorders and reported that there is an inverse relation in the serum levels of T3 and creatine kinase (CK) in thyroid disease.

Materials & Methods: A hospital based case control study was done for 3 years. Serum creatine kinase, lactate dehydrogenase activity and serum creatinine were measured in 100 cases in age group of 20-60 years of thyroid disorders and the results obtained were compared with 100 healthy controls. Assessment of the results was done using SPSS software.

Results: The TSH level and LDH activity were higher in overt hypothyroidism. T3, T4 and CK were higher in Subclinical hypothyroidism. The difference between Subclinical and over**t** hypothyroidism in thyroid profile (TSH, T3 & T4) was found to be statistically significant ($p<0.05$); CK and LDH activity were found to be statistically insignificant differences ($p>0.05$). Serum creatinine levels were positively insignificant associated with thyroid profile TSH, T3 and T4.

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Conclusion: It can be concluded from the present study that there are elevated levels of CK, LDH enzymes and serum creatinine levels represents an indicator of cellular necrosis and tissue damage. The considerable increase in serum creatinine, CK, and LDH activity suggests that these markers can be utilised to screen people with thyroid dysfunction.

Key words: Thyroid Disorder,Creatine Kinase, Lactate Dehydrogenase, creatinine

Introduction

Thyroid hormones are essential for metabolism and energy homeostasis and participate in insulin action and glucose regulation.[i] Previous studies reported higher prevalence rates of thyroid disorders in diabetic patients compared with nondiabetic individuals, and overt hypothyroidism was frequently observed in type-2 diabetes mellitus (T2DM).[ii] Moreover, subclinical hypothyroidism (SCH), a pathological status defined as an elevated serum thyroid stimulating hormone (TSH) value with normal concentrations of free thyroid hormones,[iii] is receiving increasing concerns in recent years. Meanwhile, high levels of TSH and low levels of free Triiodothyronine (FT3) within the normal range were related to a higher risk of chronic kidney disease (CKD).[iv] Also, low level of serum FT3 was found to be independently associated with urinary protein in T2DM patients.[v]In addition to the characteristic clinical picture, hypothyroidism may be associated with a wide range of muscle disturbances varying from myalgia to a true myopathy. Muscular symptoms like weakness, myalgia, stiffness, cramps and easy fatigability are seen 30-80.0% of patients. The muscular involvement in these patients, biochemical tests such as Creatine Kinase (CK) or Creatine phosphokinase (CPK) and Lactate Dehydrogenase (LDH) can be used. Of these, CK is the most sensitive indicator and measure of muscle damage and LDH is a general indicator of tissue damage. **Prakash A et al[vi] (2007)** studied the serum creatine kinase in thyroid disorders and reported that there is an inverse relation in the serum levels of T3 and creatine kinase (CK) in thyroid disease. In hypothyroid cases with decrease serum T3 there was significant CK increase in fact that might be used as parameter for screening cases of hypothyroid. Thus, estimation of the serum CK would be extremely valuable in the screening for the hypothyroid patients. **Tayal D et al[vii] (2009)** performed a cross-sectional study of the dynamic changes in biochemical markers of renal function with thyroid status in Indian population and observed the serum creatinine was significantly increased in subclinical and overt hypothyroid groups as compared to euthyroid subjects. **Haque Khan A & Majumder I[viii] (2010)** studied the

serum creatinine, and uric acid of hypothyroid patients and concluded that the serum creatinine level found significantly higher in hypothyroid patients. Therefore, hypothyroidism must be considered in cases of chronic kidney disease. **Kaur V et al[ix] (2015)** studied the changes in biochemical markers of renal function in subclinical and overt hypothyroidism and reported that a statistically significant rise in the levels of urea and creatinine in patients with subclinical and overt hypothyroidism as compared to euthyroid subjects. Additionally, in patients with overt hypothyroidism, a positive association has been found between the rise in TSH levels and creatinine. Patients with overt hypothyroidism have been found to have statistically higher uric acid levels than healthy controls. In spite of such an extensive research work and international data available with regards to the relationship between creatine kinase, lactate dehydrogenase activity and serum creatinine in diagnosed case of thyroid dysfunction patients in recent past from our geographical region that emphasizes the significance of such a novel. So, the present study was aimed to evaluate and analyse creatine kinase, lactate dehydrogenase activity and serum creatinine in diagnosed case of thyroid and control subjects.

Aim:

The aim of the present study to evaluate and analyze creatine kinase, lactate dehydrogenase activity and serum creatinine in diagnosed case of thyroid and control subjects

Materials and Methods:

The present **c**ase- control study conducted evaluate a study of thyroid function test, CK, LDH, and creatinine in thyroids dysfunction and controls subjects in the Department of Biochemistry L.N Medical College and J.K hospital, Bhopal (M.P.), India. The total sample size=200 (100 cases and 100 controls). Under aseptic condition, 3ml of venous blood was collected from the subjects in a plain vial. For measuring T3,TSH the ELISA kit from Phoenix Pharmaceuticals (Burlingame, CA, USA) was used. Estimation of serum creatine kinase (CK) by IFCC method. Estimation of serum lactate dehydrogenase (LDH) by UV - Kinetic method: Estimation of serum creatinine level by jaffe's method. Microsoft Excel was used in creating the database and producing graphs, while the data were analysed using the Statistical Package for the Social Sciences (SPSS) version 23.0 for Windows.

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Result:

Table 1: Age group distribution

Age Group (Years)	Group		Chi Square value	P value
	Hypothyroidism (n=100)	Control (n=100)		
21-30	32 (32.0%)	20 (20.0%)	17.177	**0.009**
31-40	21 (21.0%)	26 (26.0%)		
41-50	28 (28.0%)	31 (31.0%)		
51-60	19 (19.0%)	23 (23.0%)		

* chi-square ($\chi 2$) test

Majority of the studied cases were fallen in age group 41 – 50 years. We found that the statistically significant younger age population in Hypothyroidism distribution in compare to control group ($P<0.05$).

Table 2: Thyroid profile, CK, LDH and Serum Creatinine levels in Hypothyroidism, Hyperthyroidism and Control group

		Frequency	Mean	Std. Deviation	F value	P value
TSH (mlU/L)	**Hypothyroidism**	100	17.77	34.06	21.338	**<0.001**
	Control group	100	1.94	1.09		
T3 (ng/ml)	**Hypothyroidism**	100	0.86	0.41	31.736	**<0.001**
	Control group	100	1.27	0.34		
T4 (ug/dl)	**Hypothyroidism**	100	6.92	2.76	4.020	**0.019**
	Control group	100	7.66	1.38		
CK (U/L)	**Hypothyroidism**	100	201.51	47.29	302.978	**<0.001**
	Control group	100	98.11	23.87		
LDH (U/L)	**Hypothyroidism**	100	243.44	60.56	223.970	**<0.001**
	Control group	100	133.19	22.89		
Serum Creatinine (mg/dl)	**Hypothyroidism**	100	1.13	0.69	8.436	**<0.001**
	Control group	100	0.84	0.29		

* One Way ANOVA T- test

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Table 3: Thyroid profile, CK, Serum Creatinine and LDH activity distribution in various thyroid dysfunction and control groups

Parameters		Frequency	Mean	Std. Deviation	F value	P value
TSH (mlU/L)	Subclinical hypothyroidism	72	9.87	2.39	27.902	<**0.001**
	Overt hypothyroidism	26	40.41	62.10		
	Control	100	1.94	1.09		
T3 (ng/ml)	Subclinical hypothyroidism	72	1.03	0.33	36.624	<**0.001**
	Overt hypothyroidism	26	0.38	0.17		
	Control	100	1.27	0.34		
T4 (ug/dl)	Subclinical hypothyroidism	72	8.45	0.95	145.728	<**0.001**
	Overt hypothyroidism	26	2.59	1.14		
	Control	100	7.66	1.38		
CK (U/L)	Subclinical hypothyroidism	72	203.02	43.82	141.113	<**0.001**
	Overt hypothyroidism	26	198.51	57.97		
	Control	100	98.11	23.87		
LDH (U/L)	Subclinical hypothyroidism	72	241.04	59.71	103.472	<**0.001**
	Overt hypothyroidism	26	249.40	65.84		
	Control	100	133.19	22.89		
Serum Creatinine (mg/dl)	Subclinical hypothyroidism	72	1.09	0.77	4.887	<**0.001**
	Overt hypothyroidism	26	1.23	0.44		
	Control	100	0.84	0.29		

* One Way ANOVA t test

Table 4: Compare Thyroid profile, CK, LDH activity and serum creatinine level distribution in Subclinical and Overt hypothyroidism

	Hypothyroidism	Frequency	Mean	Std. Deviation	t value	P value
TSH (mlU/L)	**Subclinical**	74	9.81	2.42	4.269	**<0.001**
	Overt	26	40.41	62.10		
T3 (ng/ml)	**Subclinical**	74	1.03	0.33	9.692	**<0.001**
	Overt	26	0.38	0.17		
T4 (ug/dl)	**Subclinical**	74	8.43	0.94	25.781	**<0.001**
	Overt	26	2.59	1.14		
CK (U/L)	**Subclinical**	74	202.56	43.33	0.374	0.709
	Overt	26	198.51	57.97		
LDH (U/L)	**Subclinical**	74	241.34	58.92	0.581	0.563
	Overt	26	249.40	65.84		
Serum Creatinine (mg/dl)	**Subclinical**	74	1.09	0.76	0.893	0.374
	Overt	26	1.23	0.44		

* One Way ANOVA t test

In this table we noted the TSH level and LDH activity were higher in overt hypothyroidism; while T3, T4 and DK were higher in Subclinical hypothyroidism. The difference between Subclinical and over**t** hypothyroidism in thyroid profile (TSH, T3 & T4) was found to be statistically significant ($p<0.05$); but CK and LDH activity were found to be statistically insignificant differences ($p>0.05$).

Table 5: Correlation of Thyroid profile, CK, LDH activity and serum creatinine level

Correlations							
Pearson's Correlation Coefficient		**TSH**	**T3**	**T4**	**CK**	**LDH**	**Serum Creatinine**
TSH	**r**	1.000	-0.201**	-0.269**	0.282**	0.299**	0.017
	P value	--	**<0.001**	**<0.001**	**<0.001**	**<0.001**	0.766
T3	**r**	-0.201**	1.000	0.317**	-0.238**	-0.227**	0.030
	P value	**<0.001**	--	**<0.001**	**<0.001**	**<0.001**	0.602
T4	**r**	-0.269**	0.317**	1.000	-0.102	-0.137*	0.031
	P value	**<0.001**	**<0.001**	--	0.077	**0.018**	0.592
CK	**r**	0.282**	-0.238**	-0.102	1.000	0.813**	0.046
	P value	**<0.001**	**<0.001**	0.077	--	**<0.001**	0.425
LDH	**r**	0.299**	-0.227**	-0.137*	0.813**	1.000	0.107
	P value	**<0.001**	**<0.001**	**0.018**	**<0.001**	--	0.065

Serum Creatinine		0.017	0.030	-0.031	0.046	0.107	1.000
		0.766	0.602	0.592	0.425	0.065	--
**. Correlation is significant at the 0.01 level (2-tailed).							
*. Correlation is significant at the 0.05 level (2-tailed).							

* Bivariate analysis (Pearson's correlation coefficient)

Above table represent the Pearson Correlation (Bivariate analysis) of thyroid profile, CK and LDH activity and observed a significant association of thyroid profile TSH, T3, T4, CK and LDH activity was significant associated with each other's. Negative sign shows the universally proportional correlation.

Discussion

In this study majority of the studied cases were fallen in age group 41 – 50 years. We noted that the average age of Hypothyroidism, Hyperthyroidism and control group was 39.62±11.39, 45.57±10.81 and 42.87±11.16 years respectively. There were statistically significant higher older age population in Hyperthyroidism group and younger age population in Hypothyroidism distribution in compare to control group (P<0.05). **Shanti T et al**[x] reported that majority of the cases was belonging to 31-40 years; with mean age 35.4±9.2 years in hypothyroids and 36.2±9.8 years in control group. Contrast to our study **Tejomani M et al**[xi] reported the average age of Hypothyroidism was 33.96±10.17 and Euthyroid Controls 33.96±10.17 years. **McGrowder et al**[xii] reported the patient groups (overt hypothyroidism and subclinical hypothyroidism; overt hyperthyroidism and subclinical hyperthyroidism) and control groups were similar in regard to age (60.67 ± 17.96 and 59.16 ± 21.16; 58.38±18.33 and 58.65 ± 17.91 years) and 52.75 ± 16.44 years, respectively. In our study case groups, Hypothyroidism 61.0% and Hyperthyroidism 46.0% were female and rest were male; but in control groups 67.0% were male and 33.0% were female patients. By using the chi square test, we find insignificant distribution in both groups (P<0.05). Greater than 75.0% cases were married in present study. We noted that there was marital status distribution was statistically insignificant distribution in among groups (P>0.05). **Shanti T et alError! Bookmark not defined.** reported that gender distribution among the study subjects. Of the 50 subjects with overt hypothyroidism, 36 were females and 14 were males. In the euthyroid control group, there were 31 females and 19 males. It is evident that hypothyroidism is more predominant in females. **Tejomani M et al**Error! Bookmark not defined. reported the prevalence of hypothyroidism was higher among females as is observed worldwide. In our study we noted the TSH level and LDH activity were higher in overt hypothyroidism; while T3, T4 and CK were higher in Subclinical hypothyroidism. The difference between Subclinical and over**t** hypothyroidism in thyroid profile (TSH, T3 & T4) was found to be statistically significant (p<0.05); but CK and LDH activity were found to be statistically insignificant differences (p>0.05). On applying the bivariate analysis (Pearson's correlation) we noted a positive significant association of thyroid profile TSH with CK and LDH activity. T3 and T4 was negative significant associated. While serum creatinine was positively insignificant correlated with thyroid profile TSH, T3 and T4. **Reena R et al**Error!

Bookmark not defined. observed that the significant difference in serum CK and LDH activities were observed in these seven cases compared to rest of the forty-three cases.
Even though there was no significant difference among the study groups (cases and controls), a weak positive correlation of CK, LDH with TSH levels and weak negative correlation with T3 and T4 levels were observed. We noted the CK level 104.05±22.80U/L was higher in Subclinical hyperthyroidism in compare to in Overt hyperthyroidism group the CK level 110.21±24.64U/L was higher in compare to control group 98.11±23.87U/L. And the CK level 198.51±57.97U/L were higher in Overt hypothyroidism in compare to control group 98.11±23.87U/L. The difference between subclinical, overt thyroid dysfunction and control group in CK was found to be statistically significant ($p<0.05$). **Vaitla P et al**[xiv] reported the serum CPK levels in Hyperthyroid patients is significantly decreased compare to controls. Our study noted the LDH activity level 144.18±27.05U/L was higher in Subclinical hyperthyroidism in compare to in Overt hyperthyroidism group the LDH activity level 151.32±25.48U/L was higher in compare to control group 133.19±22.89U/L. And the LDH activity level 249.40±65.84U/L was higher in Overt hypothyroidism in compare to control group 133.19±22.89U/L. The difference between overt hypothyroidism and control group in thyroid profile LDH activity was found to be statistically significant ($p<0.05$). In a similar study **Shanti R et al**[x] serum LDH activity is significantly elevated in overt hypothyroid cases (346±33.8) compared to euthyroid controls (176.18±33.64) with a p value of <0.001 and also shows a weak positive correlation with TSH ($r= 0.331$, $p=0.018$). **Fleisher GA et al**[xv] has also found that 37% of hypothyroid patients have raised LDH levels and in other studies by **McGrowder DA et al**[xii] and **Strasberg GD**[xvi], elevation of LDH activity was found in 33% and 74% of patients with overt hypothyroidism respectively. In present study we noted the serum creatinine level 1.13±0.72 mg/dl was higher in Subclinical hyperthyroidism in compare to in Overt hyperthyroidism group the serum creatinine level 1.33±0.93 mg/dl was higher in compare to control group 0.84±0.29 mg/dl. The difference between Subclinical hypothyroidism and control group in serum creatinine was found to be statistically significant ($p<0.05$). We also noted the serum creatinine level 1.23±0.44mg/dl were higher in Overt hypothyroidism in compare to control group 1 0.84±0.29 mg/dl. The difference between overt hypothyroidism and control group serum creatinine in was found to be statistically significant ($p<0.05$). **Patil VP et al**[xvii] reported the creatinine were higher in subclinical hypothyroid than control euthyroidism (ET) ($P<0.001$). It can be concluded from the present study that there are elevated levels of CK, LDH enzymes and serum creatinine levels represents an indicator of cellular necrosis and tissue damage. Hence Hypothyroidism should be considered in patients with myopathy and unexplained elevation of serum muscle enzymes.

Conclusion

It can be concluded from the present study that there are elevated levels of CK, LDH enzymes and serum creatinine levels represents an indicator of cellular necrosis and tissue damage. Hence Hypothyroidism should be considered in patients with myopathy and unexplained elevation of serum muscle enzymes. According to this study, hypothyroidism is common in the third & fourth decade of life. Female is more affected than the male.

Therefore, it may be inferred that CPK and aldolase readings may serve as a supplemental diagnostic tool for the identification of hypothyroid diseases and may also suggest as a useful prognostic metric. The considerable increase in serum creatinine, CK, and LDH activity suggests that these markers can be utilised to screen people with thyroid dysfunction. Gradually increasing hypothyroid patients are creating a burden on health care centres 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.

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