

Assessment of Serum Creatine Kinase (CK) and Lactate Dehydrogenase (LDH) Levels in Patients with Thyroid Disorders: A Hospital-Based Study from Bihar

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Abstract:

Background: Thyroid dysfunctions are among the most common endocrine disorders worldwide, with hypothyroidism and hyperthyroidism producing systemic metabolic effects. Thyroid hormones influence nearly all metabolic pathways, and their imbalance often leads to muscular involvement. Serum enzyme markers such as **Creatine Kinase (CK)** and **Lactate Dehydrogenase (LDH)** reflect these muscular and metabolic changes and may serve as useful adjuncts in evaluating thyroid disease severity.

Aim: To evaluate and compare serum levels of CK and LDH in patients with thyroid disorders and healthy controls, and to assess their correlation with thyroid hormone levels (TSH, T3, and T4).

Methods: This **prospective observational study** was conducted in the Departments of Biochemistry and Endocrinology, IGIMS, Patna, over a period of 18 months (February 2020–July 2021). A total of **150 participants** were enrolled, including **100 cases** (70 hypothyroid, 30 hyperthyroid) and **50 age- and sex-matched healthy controls**. Serum TSH, total T3, and T4 were estimated by **Chemiluminescent Microparticle Immunoassay (CMIA)** on Abbott Architect i2000SR, while CK and LDH were measured using **Beckman Coulter AU5800** based on the IFCC method. Data were analyzed using **SPSS version 23.0**, applying t-tests, ANOVA, and Pearson's correlation, with $p < 0.05$ considered statistically significant.

Results: The mean serum **TSH** was significantly higher in hypothyroid patients (18.9 ± 9.4 μ IU/mL) and lower in hyperthyroid patients (0.16 ± 0.08 μ IU/mL) compared to controls (2.6 ± 1.2 μ IU/mL). Serum **CK** and **LDH** levels were markedly elevated in hypothyroid patients (246.8 ± 88.6 IU/L and 384.5 ± 105.4 IU/L, respectively) compared to controls (109.2 ± 42.3 IU/L and 172.4 ± 33.7 IU/L; $p < 0.001$). Hyperthyroid patients showed decreased CK (78.4 ± 29.1 IU/L) but mildly elevated LDH (265.7 ± 58.2 IU/L). CK and LDH correlated positively with TSH ($r = +0.74$ and $+0.61$, respectively) and negatively with T3 and T4 levels ($p < 0.001$).

Conclusion: Serum CK and LDH levels are significantly increased in hypothyroid patients, indicating skeletal muscle involvement and metabolic disturbance. These enzymes correlate

strongly with thyroid dysfunction severity and may serve as valuable adjuncts in assessing muscular and metabolic changes associated with thyroid disorders.

Recommendations: Routine estimation of CK and LDH in thyroid patients is recommended to detect early myopathic involvement, monitor disease progression, and assess treatment response, particularly in overt hypothyroidism.

Keywords: Thyroid disorders; Hypothyroidism; Creatine kinase; Lactate dehydrogenase; Muscle enzymes.

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Introduction

Thyroid disorders are among the most prevalent endocrine abnormalities worldwide, affecting almost every organ system through alterations in metabolism, growth, and energy regulation. According to recent epidemiological surveys, nearly **42 million people in India** are estimated to suffer from various thyroid dysfunctions, making it a significant public health concern [1]. These disorders are broadly classified into **hypothyroidism** and **hyperthyroidism**, each characterized by distinct clinical and biochemical profiles that influence metabolic processes and tissue function [2].

Thyroid hormones play a crucial role in maintaining basal metabolic rate, regulating mitochondrial activity, and controlling protein and carbohydrate metabolism. Consequently, any deviation from normal thyroid function impacts tissues with high energy demand, including skeletal and cardiac muscles [3]. In **hypothyroidism**, a reduction in thyroid hormones leads to decreased mitochondrial oxidative activity, impaired energy metabolism, and accumulation of mucopolysaccharides in muscles, resulting in myopathy and elevated serum muscle enzymes such as **(CK)** and **(LDH)** [4]. In contrast, **hyperthyroidism** enhances metabolic turnover, which may lead to altered enzyme activity but not always associated with overt muscle damage [5].

Elevations in CK and LDH have been recognized as indicators of muscle involvement in thyroid dysfunctions. These enzymes serve as sensitive biochemical

markers reflecting subclinical myopathic changes before the appearance of overt clinical symptoms [6]. Recent studies have emphasized that increased CK and LDH levels correlate positively with thyroid-stimulating hormone (TSH) concentration and negatively with circulating thyroid hormones (T3, T4), suggesting their potential diagnostic and prognostic value in thyroid disorders [7].

Despite advancements in thyroid hormone assays, enzyme markers remain underutilized in routine evaluation of thyroid disease, particularly in resource-limited settings. A systematic assessment of CK and LDH in patients with thyroid dysfunction can provide additional insights into the extent of tissue involvement, especially in hypothyroid myopathy [8].

The present study was undertaken to evaluate and compare serum CK and LDH levels in patients with thyroid disorders and healthy controls and to analyze their correlation with thyroid hormone levels. This hospital-based study from Bihar aims to highlight the diagnostic utility of these biochemical markers as adjunct tools in assessing **muscle involvement and metabolic alterations** in thyroid dysfunction.

Methodology

Study Design

This was a prospective observational study.

Study Setting

The study was carried out jointly in the Department of Biochemistry and the Department of Endocrinology, Indira Gandhi Institute of Medical Sciences (IGIMS), Patna, Bihar. All laboratory investigations were performed in the Clinical Biochemistry Laboratory, IGIMS.

Study Duration

The total duration of the study was **18 months**, extending from **February 2020 to July 2021**.

Study Participants

A total of **150 participants** were included in the study. Out of these, **100 were cases** diagnosed with thyroid disorders (both hypothyroidism and hyperthyroidism) attending the Endocrinology OPD, and **50 were age- and sex-matched healthy individuals** serving as controls. Written informed consent was obtained from all participants prior to inclusion in the study.

Inclusion Criteria

- Patients aged between **18 and 60 years**.
- Clinically and biochemically diagnosed cases of thyroid disorders (hypothyroidism or hyperthyroidism) with or without symptoms of muscular involvement.
- Participants' willingness.

Exclusion Criteria

- Patients with cardiovascular diseases, hypertension, diabetes mellitus, neuromuscular disorders, recent stroke, or epilepsy.
- Individuals on medications known to alter enzyme activity such as **beta-blockers, statins, lithium, steroids, fibrates, and phenothiazines**.
- Those with hepatic, renal, or pulmonary insufficiency.
- Individuals with recent trauma, strenuous exercise, or intramuscular injections.
- Pregnant or lactating women.
- Patients positive for **HIV, Hepatitis B, or Hepatitis C** infection.

Bias and Confounding Factors

To minimize selection bias, participants were selected consecutively from the outpatient department based on inclusion and exclusion criteria. Laboratory personnel performing biochemical analyses were blinded to the clinical status of participants. Pre-analytical variability was minimized by collecting all samples under standardized fasting conditions in the morning.

Data Collection

Data were collected using a pre-designed proforma including demographic information, clinical history, physical findings (such as pulse, blood pressure, thyroid swelling, BMI), and biochemical results. **Five milliliters of fasting venous blood** were drawn under aseptic conditions, allowed to clot, and centrifuged to obtain serum for analysis.

Procedure

Serum **TSH, total T3, and total T4** were estimated using **Chemiluminescent Microparticle Immunoassay (CMIA)** on the **Abbott Architect i2000SR** analyzer. Serum **CK and LDH** were measured spectrophotometrically using **Beckman Coulter AU5800 automated analyzer** based on the **modified IFCC method**. Grossly hemolyzed samples were excluded. All samples were analyzed within 48 hours or stored at -20°C until analysis.

Statistical Analysis

Data were compiled and analyzed using **(SPSS) version 23.0**. Continuous variables were expressed as mean $\pm$ standard deviation (SD). Differences between cases and controls were analyzed using the **Student's t-test**. Correlation between biochemical parameters (TSH, T3, T4, CK, LDH) was determined using **Pearson's correlation coefficient (r)**. A p-value < 0.05 was considered statistically significant.

Results

1. Study Population

The study included **150 subjects**, divided into three groups:

- **Group I:** Hypothyroid patients (n = 70)
- **Group II:** Hyperthyroid patients (n = 30)

- **Group III:** Healthy controls (n = 50)

The participants' ages ranged from **18 to 60 years**, with a mean of **38.6 ± 10.4 years**. Females constituted the majority (71.3%) in both cases and controls.

Table 1: Demographic Profile of Study Subjects

Parameter	Hypothyroid (n=70)	Hyperthyroid (n=30)	Controls (n=50)	F / χ^2 value	p-value
Age (years, Mean ± SD)	39.8 ± 9.8	37.5 ± 10.6	36.7 ± 10.3	1.04	0.35 (NS)
Male: Female	18: 52	9: 21	16: 34	0.49	0.61 (NS)
BMI (kg/m ² , Mean ± SD)	24.62 ± 2.89	23.12 ± 2.31	22.43 ± 2.05	4.16	0.02*

*NS = Not significant; p < 0.05 = statistically significant.

Most of the participants were women in the 30–50-year age group. Hypothyroid patients showed slightly higher BMI values compared to other groups.

The thyroid hormone profile (TSH, T3, and T4) differed significantly among the three groups. Hypothyroid patients had elevated TSH and reduced T3 and T4, while hyperthyroid patients showed the opposite trend.

2. Thyroid Profile

Table 2: Thyroid Hormone Levels Among Study Groups

Parameter	Controls (n=50)	Hypothyroid (n=70)	Hyperthyroid (n=30)	F-value	p-value
TSH (μIU/mL)	2.58 ± 1.22	18.94 ± 9.43	0.16 ± 0.08	269.4	<0.001***
Total T3 (ng/mL)	1.09 ± 0.18	0.44 ± 0.14	3.82 ± 0.91	305.2	<0.001***
Total T4 (μg/dL)	8.41 ± 1.85	3.76 ± 1.48	16.90 ± 3.84	281.3	<0.001***

p < 0.001 = Highly significant.

The mean serum TSH was approximately **sevenfold higher** in hypothyroid patients, while total T3 and T4 were markedly elevated in hyperthyroid patients compared to controls.

3. Serum Creatine Kinase (CK) and Lactate Dehydrogenase (LDH)

Serum CK and LDH values were obtained from all subjects. In the **control group (n=50)**, based on the data obtained:

- Mean **CK** = **109.2 ± 42.3 IU/L** (Range: 38.5–212.9)
- Mean **LDH** = **172.4 ± 33.7 IU/L** (Range: 106.4–248.0)

Hypothyroid subjects demonstrated significantly higher levels of CK and LDH, whereas hyperthyroid subjects showed decreased CK but mildly elevated LDH compared to controls.

Table 3: Comparison of Serum CK and LDH Levels

Parameter	Controls (n=50)	Hypothyroid (n=70)	Hyperthyroid (n=30)	F-value	p-value
CK (IU/L)	109.2 ± 42.3	246.8 ± 88.6	78.4 ± 29.1	81.9	<0.001***
LDH (IU/L)	172.4 ± 33.7	384.5 ± 105.4	265.7 ± 58.2	55.6	<0.001***

p < 0.001 = Highly significant.

Hypothyroid patients exhibited a **2.3-fold increase in CK** and **~2.2-fold increase in LDH** compared to controls, reflecting significant muscular involvement. Hyperthyroid cases had reduced CK but mildly increased LDH, possibly due to hepatic enzyme induction.

4. Subgroup Analysis of Hypothyroid Patients

Among the hypothyroid group, **50 patients (71%)** had overt hypothyroidism and **20 (29%)** had subclinical hypothyroidism. Both CK and LDH levels were significantly higher in overt hypothyroid cases.

Table 4: Overt vs. Subclinical Hypothyroidism

Parameter	Subclinical (n=20)	Overt (n=50)	t-value	p-value
TSH (μIU/mL)	8.7 ± 2.6	27.5 ± 9.8	12.2	<0.001***
CK (IU/L)	164.5 ± 47.2	282.7 ± 93.8	6.7	<0.001***
LDH (IU/L)	322.4 ± 75.5	416.3 ± 108.9	4.6	<0.001***

Elevation of muscle enzymes was more pronounced in overt hypothyroidism, supporting the role of thyroid hormones in skeletal muscle metabolism.

5. Correlation Between Thyroid Hormones and Muscle Enzymes

Correlation analysis revealed significant relationships between thyroid hormones and enzyme activities.

A **positive correlation** was found between **TSH and CK (r = +0.74, p < 0.001)** and **TSH and LDH (r = +0.61, p < 0.001)**.

Negative correlations were observed between T3 and both CK (r = -0.56) and LDH (r = -0.48).

Table 5: Pearson Correlation Coefficients Between Thyroid and Enzyme Parameters (n = 100 Cases)

Parameter	TSH	T3	T4
CK	+0.74*	-0.56*	-0.61*
LDH	+0.61*	-0.48	-0.53

*p < 0.05 = significant, **p < 0.01, ***p < 0.001 = highly significant.

Higher TSH levels were associated with greater elevation of CK and LDH, reflecting muscle cell damage in hypothyroid states.

6. Summary of Results

- Out of 150 subjects, 100 were thyroid disorder cases (70 hypothyroid, 30 hyperthyroid) and 50 were controls.
- Hypothyroid patients showed **significantly elevated** serum CK and LDH levels (p < 0.001).

- Hyperthyroid patients exhibited **reduced CK** but **moderately raised LDH**.
- Strong correlations were found between **TSH and muscle enzyme levels**.
- Overt hypothyroidism demonstrated the **highest enzyme elevation**, suggesting direct muscular involvement.

Discussion

A total of **150 participants** were enrolled in this prospective observational study, including **100 patients with thyroid disorders** (70 hypothyroid and 30 hyperthyroid) and **50 age- and sex-matched healthy controls**. The majority of the study participants were females (71.3%), which aligns with the well-established female predominance in thyroid disorders. The mean age of the subjects was **38.6 ± 10.4 years**, reflecting that thyroid dysfunction is more prevalent in the middle-aged population.

The **BMI** was significantly higher among hypothyroid patients compared to controls and hyperthyroid subjects. This observation is consistent with the reduced basal metabolic rate and altered lipid and carbohydrate metabolism in hypothyroidism, which often lead to weight gain and increased adiposity.

A clear biochemical distinction among the three study groups was evident in the thyroid profile. Mean serum **TSH** levels were markedly elevated in hypothyroid patients (**18.9 ± 9.4 μ IU/mL**) and significantly suppressed in hyperthyroid patients (**0.16 ± 0.08 μ IU/mL**) compared to controls (**2.6 ± 1.2 μ IU/mL**). Conversely, mean **T3** and **T4** levels were decreased in hypothyroid and elevated in hyperthyroid subjects. These results confirm the successful categorization of participants according to their thyroid function status and the reliability of laboratory diagnostic criteria used in the study.

When comparing serum muscle enzymes, the findings were highly significant. The **mean CK activity** in hypothyroid patients

(**246.8 ± 88.6 IU/L**) was more than twice the level seen in controls (**109.2 ± 42.3 IU/L**), whereas hyperthyroid patients had lower CK activity (**78.4 ± 29.1 IU/L**). Similarly, **LDH activity** was substantially higher in hypothyroid patients (**384.5 ± 105.4 IU/L**) compared to both controls (**172.4 ± 33.7 IU/L**) and hyperthyroid subjects (**265.7 ± 58.2 IU/L**). These elevations in enzyme activities suggest significant **skeletal muscle involvement** and altered cellular metabolism in hypothyroidism, while hyperthyroidism may induce mild hepatic enzyme stimulation but not substantial muscle damage.

A **subgroup analysis** of hypothyroid patients revealed that those with **overt hypothyroidism** had markedly higher CK and LDH levels than patients with subclinical hypothyroidism. This graded increase in enzyme levels with the severity of thyroid hormone deficiency strongly supports the role of thyroid hormones in maintaining normal muscle integrity and mitochondrial function. The findings are consistent with previous studies showing that myopathy and enzyme leakage are more pronounced in overt hypothyroidism.

Correlation analysis demonstrated a **strong positive relationship between TSH and both CK ($r = +0.74$) and LDH ($r = +0.61$)**, along with a **significant negative correlation between thyroid hormones (T3, T4) and these enzymes**. This inverse relationship suggests that decreased thyroid hormone availability leads to impaired oxidative metabolism and subsequent muscle cell membrane damage, resulting in enzyme leakage into circulation.

Several studies have demonstrated that serum (CK) and (LDH) levels are altered in patients with thyroid dysfunction. Kumar et al. [9] observed that hypothyroid patients exhibit significantly elevated CK and LDH levels, reflecting reduced metabolism and impaired clearance of muscle enzymes. In contrast, hyperthyroid patients showed variable or mildly decreased CK levels.

These findings suggest a correlation between thyroid hormone levels and enzyme activity, indicating the potential of CK and LDH as biomarkers for thyroid dysfunction. Elevated CK levels in hypothyroid patients have also been linked to subclinical myopathy. Reddy et al. [10] reported that CK activity in hypothyroid individuals reflects early muscular involvement, even in the absence of overt symptoms. This reinforces the role of CK as a sensitive marker for muscle injury secondary to thyroid hormone deficiency.

LDH has been suggested as a marker of broader metabolic stress in thyroid disorders. Gowda et al. [11] found that LDH isoenzyme patterns shift in hypothyroid patients, indicating tissue involvement beyond skeletal muscle, including hepatic and cardiac tissues. This underscores the systemic nature of enzymatic alterations in thyroid dysfunction. Therapeutic normalization of thyroid hormone levels has been shown to restore CK and LDH to reference ranges. Prajapati et al. [12] reported that treatment of hypothyroidism led to the normalization of both enzymes, confirming the direct association between thyroid hormone levels and enzymatic activity.

Even subclinical hypothyroidism may cause modest increases in serum CK and LDH. Sahoo et al. [13] demonstrated that patients with mild thyroid hormone deficiency exhibited significant but subtle elevations of these enzymes, suggesting early muscular and metabolic stress that may precede overt clinical symptoms. Finally, comparative studies indicate differential enzyme patterns in hypo- and hyperthyroidism. Zhang et al. [14] highlighted that CK elevation is predominantly seen in hypothyroidism, whereas LDH may rise in both hypo- and hyperthyroid states, reflecting broader tissue injury. These findings support the utility of LDH as a more general marker of systemic metabolic stress in thyroid disorders.

Conclusion

The present study demonstrates that **serum (CK) and (LDH) levels** are significantly elevated in patients with **hypothyroidism**, particularly in overt cases, indicating notable **muscle involvement** due to thyroid hormone deficiency. In contrast, **hyperthyroid patients** showed reduced CK and mildly increased LDH levels. A strong positive correlation between **TSH** and both **CK** and **LDH**, along with a negative correlation with **T3** and **T4**, suggests that these enzymes can serve as valuable **biochemical indicators of thyroid dysfunction severity**. Routine estimation of CK and LDH may aid in assessing **metabolic and muscular alterations** in patients with thyroid disorders.

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