ORIGINAL ARTICLE

# Serum CPK and Serum Creatinine Levels in Patients of Hypothyroidism

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## Abstract

**Background:** Thyroid hormone profoundly influences metabolic processes. Hypothyroidism, a common endocrine disorder, can significantly impact skeletal muscle and renal function. In hypothyroidism, muscle involvement often manifests as myopathy with elevated serum creatine phosphokinase (CPK) levels, while renal effects may alter serum creatinine levels and glomerular filtration rate. However, the extent of these changes and their relationship to hypothyroidism severity, especially in subclinical cases, remains unclear. This study aimed to evaluate these parameters in overt and subclinical hypothyroidism and investigate their correlation with thyroid function.

**Materials and methods:** This cross-sectional study included 150 patients with hypothyroidism attending the Medicine OPD at Gandhi Medical College and Hamidia Hospital, Bhopal. Patients were divided into two groups: Group A with overt hypothyroidism and group B with subclinical hypothyroidism, based on their thyroid function tests. Serum levels of thyroid-stimulating hormone (TSH), free $T_3$, free $T_4$, CPK, and creatinine were measured for all participants. Creatinine clearance was calculated using the Cockcroft-Gault formula. Statistical analysis included *t*-tests for group comparisons and Pearson correlation to assess relationships between variables.

**Results:** Serum CPK levels were significantly higher in overt hypothyroidism compared with subclinical hypothyroidism ($p < 0.001$). Similarly, serum creatinine levels were significantly elevated in overt hypothyroidism compared with subclinical cases ($p < 0.001$). A positive correlation was observed between serum TSH and CPK ($r = 0.435$, $p < 0.001$) and between TSH and creatinine ($r = 0.208$, $p = 0.011$). Serum $T_4$ showed negative correlations with both CPK ($r = –0.363$, $p < 0.001$) and creatinine ($r = –0.546$, $p < 0.001$).

**Conclusion:** This study demonstrates that both serum CPK and creatinine levels are significantly elevated in hypothyroidism, particularly in overt cases. The strong correlations between thyroid function tests and these parameters suggest that CPK and creatinine could serve as useful markers for assessing hypothyroidism severity and monitoring treatment response.

**Keywords:** Creatine phosphokinase, Creatinine, Hypothyroidism, Muscle enzymes, Renal function, Thyroid-stimulating hormone.

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## Background

Thyroid hormones, produced by the thyroid gland, play a crucial role in regulating metabolism, growth, and development throughout the body.[1] Hypothyroidism, a common endocrine disorder, results from insufficient production or action of thyroid hormones. It affects ~ 11% of the Indian population, with significant variations across different regions.[2,3] It can present in two stages or severities: Overt hypothyroidism, characterized by elevated thyroid-stimulating hormone (TSH) and decreased free thyroxine ($T_4$) levels, often accompanied by clear symptoms, and subclinical hypothyroidism, where TSH is mildly elevated but free $T_4$ remains within the normal range, typically with minimal or no symptoms.[4]

Thyroid hormones significantly influence skeletal muscle physiology, including contractile function, myogenesis, and metabolism.[5] In hypothyroidism, muscle involvement often manifests as myopathy, characterized by weakness, fatigue, and reduced exercise tolerance.[6] These changes are often accompanied by elevated serum creatine phosphokinase (CPK) levels, a marker of muscle damage.[7] The extent of CPK elevation and its correlation with the severity of hypothyroidism, particularly in subclinical cases, remains a subject of ongoing research in the Indian context.

Thyroid dysfunction can also have profound effects on renal function. In hypothyroid states, reduced thyroid hormone levels can lead to decreased renal plasma flow, lower glomerular filtration rate (GFR), and impaired urine concentration.[8] These changes affect not only kidney hemodynamics but also tubular function and electrolyte homeostasis.[9] However, the extent of these changes and their correlation with thyroid function tests in different stages of hypothyroidism are not fully understood, especially in the Indian population.

Despite the known impacts of hypothyroidism on muscle and kidney function, the utility of serum CPK and creatinine as potential biomarkers for assessing thyroid function and monitoring treatment response has not been fully established in the Indian healthcare scenario.[10] Early detection of muscle and renal involvement in hypothyroidism could potentially improve patient management and outcomes.[11] This study aims to evaluate serum CPK and creatinine levels in patients with overt and subclinical hypothyroidism in Madhya Pradesh and investigate their correlation with thyroid function parameters, potentially providing insights into

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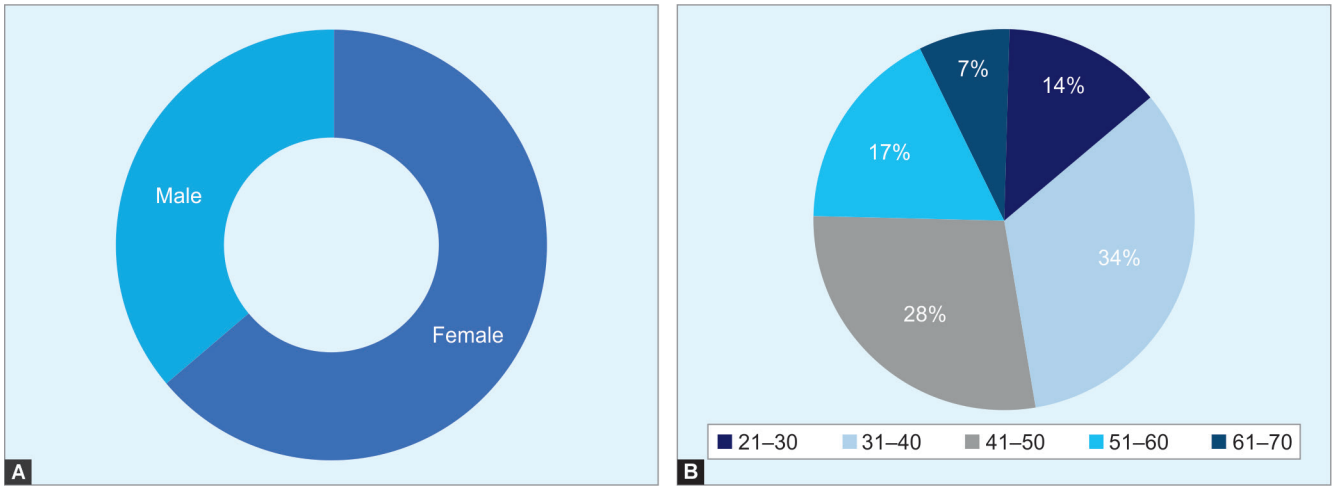
**Conflict of interest:** None




**Figs 1A and B:** Distribution of hypothyroid patients according to (A) Gender and (B) Different age-groups

**Table 1:** Distribution of serum CPK and creatinine level of cases among different types of hypothyroidism

| | *Serum CPK* | | *Serum creatinine* | |
|---|---|---|---|---|
| *Study groups* | *High (>170 U/L)* | *Mean ± SD* | *High (>1.3 mg/dL)* | *Mean ± SD* |
| Group A | 36 (64.3%) | 218.88 ± 81.86 U/L | 48 (85.7%) | 1.59 ± 0.21 mg/dL |
| Group B | 46 (48.9%) | 178.84 ± 58.73 U/L | 35 (37.2%) | 1.21 ± 0.29 mg/dL |

the systemic effects of hypothyroidism and improving diagnostic and monitoring strategies in the regional context.

## Materials and Methods

This observational, cross-sectional study was conducted at the Department of Medical Biochemistry in collaboration with the Department of Medicine, Gandhi Medical College and Hamidia Hospital, Bhopal, over an 18-month period from August 2022 to February 2024. The study included 150 patients with hypothyroidism attending the Medicine OPD. Ethical clearance was obtained from the Institutional Ethics Committee (certificate no. 32228/MC/IEC/2022), and informed consent was taken from all participants.

### Inclusion and Exclusion Criteria

Patients above 18 years of age with recently detected or poorly controlled hypothyroidism were included. Exclusion criteria encompassed patients with known impaired renal function, cardiovascular diseases, autoimmune disorders, or those on medications affecting study parameters.

### Sample Collection and Processing

Venous blood samples (5 mL) were collected from each subject, and serum was separated by centrifugation at 3000 rpm for 15 minutes. Thyroid function tests (TSH, $T_3$, $T_4$) were performed using the ELISA method. Serum CPK was measured by the modified IFCC method and serum creatinine was estimated by the Jaffe-Compensated assay using a fully automatic biochemistry analyzer (BA 400) (Fig. 1).

### Study Groups

Participants were divided into two groups based on thyroid profile: group A, overt hypothyroidism group and group B, subclinical hypothyroidism.

### Statistical Analysis

Data analysis was performed using SPSS software version 21.0. Categorical data were expressed as frequency and percentage, while continuous data were presented as mean and standard deviation. Correlation of thyroid profile with continuous variables was assessed using Pearson correlation coefficient and student's *t*-test. Chi-square test was employed to analyze the association between categorical variables. A *p*-value less than 0.05 was considered statistically significant.

## Results and Discussion

Present study included 150 hypothyroid patients, with a notable female predominance (64% females, 36% males). The majority of patients were in the 31–40 years age-group (33.3%), followed by 41–50 years (28.0%). This age and gender distribution reflects the higher prevalence of thyroid disorders in middle-aged females.

Overt hypothyroidism was observed in 37.3% of patients (group A), while 62.7% had subclinical hypothyroidism (group B). This distribution highlights the importance of screening for subclinical cases, which often precede overt hypothyroidism and may benefit from early intervention (Table 1).

The elevated CPK levels, particularly in overt hypothyroidism, can be attributed to the impact of thyroid hormone deficiency on muscle metabolism. Hypothyroidism leads to reduced protein turnover and impaired mitochondrial oxidative metabolism in skeletal muscles, potentially resulting in increased CPK leakage from muscle cells.[6] The higher prevalence of elevated CPK in overt hypothyroidism suggests a dose-dependent effect of thyroid hormone deficiency on muscle integrity (Fig. 2).[12]

Moreover, serum creatinine levels were significantly higher in group A compared with group B ($p < 0.001$). In group A, 85.7% of patients showed elevated creatinine levels, while in group B, 37.2% had elevated levels. These results align with studies by Patil et al.[13]

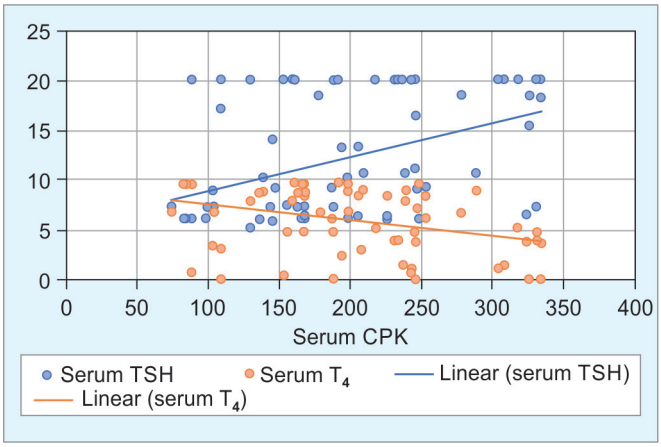



**Fig. 2:** Scatterplot diagram of correlation analysis between serum CPK with serum TSH and serum $T_4$ in patients of hypothyroidism

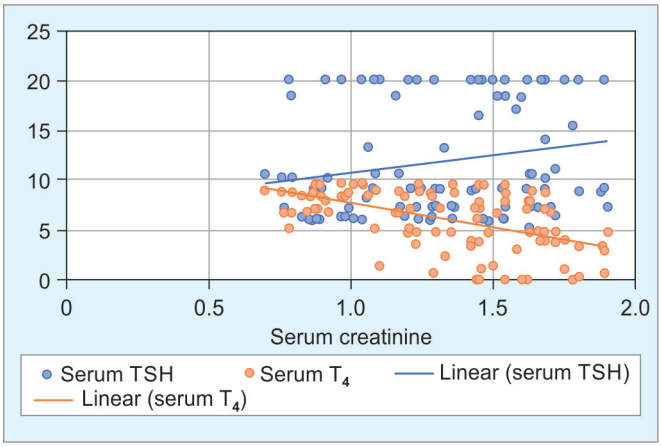



**Fig. 3:** Scatterplot diagram of correlation analysis between serum creatinine with serum TSH and serum $T_4$ in patients of hypothyroidism

and Tayal et al.,[14] who also observed increased serum creatinine in hypothyroid patients.

The elevation in serum creatinine observed in hypothyroid patients can be attributed to several interrelated mechanisms. First, hypothyroidism is associated with decreased cardiac output and increased peripheral vascular resistance, which leads to reduced renal blood flow and consequently, a decrease in GFR.[8]

This hemodynamic alteration directly impacts the kidney's ability to filter creatinine effectively. Second, thyroid hormones play a crucial role in creatine synthesis and metabolism. In hypothyroid states, this altered hormonal milieu can affect creatinine levels in the serum.[10] Lastly, the myopathy commonly associated with hypothyroidism may contribute to increased creatinine production. As muscle breakdown occurs due to hypothyroid-induced muscle weakness, more creatinine is released into the bloodstream.[15] These combined factors – reduced filtration, altered metabolism, and increased production – collectively contribute to the elevated serum creatinine levels observed in hypothyroid patients, particularly in cases of overt hypothyroidism.

A significant positive correlation was observed between serum TSH and CPK ($r = 0.435$, $p < 0.001$), and between TSH and creatinine ($r = 0.208$, $p = 0.011$). Conversely, serum $T_4$ showed negative correlations with both CPK ($r = -0.363$, $p < 0.001$) and creatinine ($r = -0.546$, $p < 0.001$). These correlations underscore the direct influence of thyroid function on both muscle integrity and renal function.

The positive correlation between TSH and CPK, along with the negative correlation between $T_4$ and CPK, suggests that the severity of hypothyroidism directly relates to the degree of muscle involvement. Similarly, the strong negative correlation between $T_4$ and creatinine levels highlights the impact of thyroid hormone deficiency on renal function. These relationships emphasize the importance of considering thyroid status when interpreting both muscle enzyme levels and renal function tests in clinical practice (Fig. 3).

The concurrent elevation of CPK and creatinine in hypothyroid patients, particularly in overt cases, suggests a complex interplay between thyroid dysfunction, muscle metabolism, and renal function. These findings emphasize the need for comprehensive evaluation of hypothyroid patients, including assessment of both muscle and renal parameters (Fig. 4).

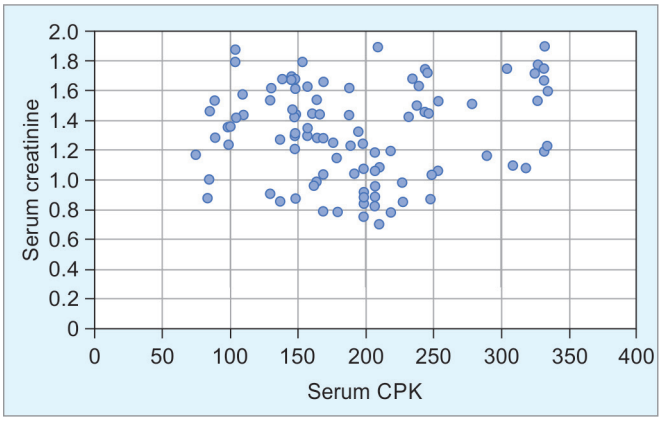



**Fig. 4:** Scatterplot diagram of correlation analysis between serum CPK and serum creatinine in patients of hypothyroidism

## Conclusion

This study demonstrates significant elevations in serum CPK and creatinine levels in hypothyroid patients, particularly in overt cases. These findings underscore the systemic impact of thyroid dysfunction on muscle integrity and renal function. The observed correlations between thyroid hormones, CPK, and creatinine highlight the intricate relationship between thyroid status and these physiological parameters. Present results emphasize the importance of comprehensive evaluation in hypothyroid patients, including regular monitoring of muscle and renal markers even in subclinical cases. This approach may facilitate early detection of complications and guide appropriate management. While providing valuable insights, this study also underscores the need for further longitudinal research to fully elucidate the long-term effects of hypothyroidism on muscle and kidney function, as well as the impact of thyroid hormone replacement therapy on these parameters.

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