



## “Study on the Occurrence of Elevated CPK Levels and Its Association with Cardiovascular Risk in Newly Diagnosed Hypothyroid Patients”

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### KEYWORDS

Hypothyroidism, Creatine Phosphokinase (CPK), Cardiovascular Risk, PROCAM Score, Thyroid Dysfunction, Biomarker

### ABSTRACT:

**Background:** Hypothyroidism, a prevalent endocrine disorder, has been associated with an increased risk of cardiovascular disease (CVD). Elevated creatine phosphokinase (CPK) levels, commonly seen in hypothyroid patients, may serve as an early marker for cardiovascular risk. This study aims to investigate the occurrence of elevated CPK levels and its association with cardiovascular risk in newly diagnosed hypothyroid patients.

**Materials and Methods:** A cross-sectional study was conducted at Aarupadai Veedu Medical College and Hospital, Puducherry, involving 100 newly diagnosed hypothyroid patients. Patients with prior thyroid treatment, history of cardiovascular disease, pregnancy, or use of medications affecting CPK levels were excluded. Demographic details, thyroid function tests (TSH, FT3, FT4), lipid profiles, and CPK levels were assessed. Cardiovascular risk was evaluated using the PROCAM score, and statistical analysis was performed using SPSS v23.0, with  $p < 0.05$  considered significant.

**Results:** The study included 100 patients (32% male, 68% female) with a mean age of  $43.2 \pm 14.7$  years. Among them, 26% were smokers and 35% had diabetes. The mean CPK level was 88.8, with a median of 46.0. Cardiovascular risk assessment showed that 36% had  $< 1\%$  risk, while 5% had  $> 40\%$  risk. A significant positive correlation was found between CPK levels and cardiovascular risk ( $r = 0.768$ ,  $p < 0.01$ ) as well as with the PROCAM score ( $r = 0.742$ ,  $p < 0.01$ ), suggesting that elevated CPK levels could indicate higher cardiovascular risk.

**Conclusion:** The study highlights a significant association between elevated CPK levels and increased cardiovascular risk in newly diagnosed hypothyroid patients. Routine monitoring of CPK levels may aid in the early identification of patients at higher risk for cardiovascular complications, allowing for timely intervention and better management of hypothyroidism-related cardiovascular risks.

### Introduction:

Hypothyroidism, a disorder marked by inadequate thyroid hormone production, is among the most common

endocrine conditions globally.<sup>1,2</sup> Hypothyroidism occurs when the thyroid gland produces insufficient amounts of thyroid hormones, particularly thyroxine (T4) and triiodothyronine (T3), which play a crucial role in



regulating metabolism, growth, and development. The global prevalence of this condition varies, with estimates suggesting that overt hypothyroidism affects around 4.6% of adults in the United States and 2% in the United Kingdom, while subclinical hypothyroidism (SCH) is far more widespread.<sup>3</sup> In India, the prevalence of hypothyroidism is alarmingly high, with recent estimates suggesting that approximately 11% of the population is affected, making it a significant public health challenge. A major concern in managing hypothyroidism is its potential to cause various complications, particularly an increased risk of cardiovascular disease (CVD), which is often exacerbated by the condition.<sup>4,5</sup>

The connection between thyroid dysfunction and cardiovascular risk is well established, as both overt and subclinical hypothyroidism contribute to an increased likelihood of developing cardiovascular disease. Thyroid hormones play a crucial role in maintaining heart function, lipid metabolism, and vascular health. In hypothyroid patients, reduced T3 and T4 levels lead to disruptions in lipid metabolism, elevated cholesterol levels, and increased blood pressure, all of which are key risk factors for cardiovascular disease.<sup>6,7</sup> Hypothyroidism is associated with endothelial dysfunction, increased arterial stiffness, and a higher risk of atherosclerosis, making individuals more susceptible to conditions such as coronary artery disease (CAD) and stroke. Additionally, it is linked to a greater prevalence of dyslipidemia, characterized by elevated low-density lipoprotein cholesterol (LDL-C) and total cholesterol levels, along with reduced high-density lipoprotein cholesterol (HDL-C) levels.<sup>8,9</sup> Hypothyroidism can contribute to an increase in left ventricular mass and reduced cardiac contractility, elevating the risk of heart failure. These cardiovascular complications are particularly concerning for individuals with coexisting conditions such as hypertension, diabetes, and obesity. In India, where lifestyle-related diseases are becoming more prevalent, hypothyroid patients face a heightened risk of cardiovascular disorders, further aggravated by urbanization, unhealthy dietary patterns, and a lack of awareness about thyroid health.<sup>10</sup>

Creatine phosphokinase (CPK), an enzyme found in the heart, brain, and skeletal muscles, is widely used as a marker of muscle damage and tissue injury. In hypothyroid individuals, particularly those with chronic or severe thyroid hormone deficiency, elevated CPK

levels are frequently observed. This increase is attributed to muscle damage caused by the lack of thyroid hormones, which play a key role in muscle function and metabolism. Hypothyroid patients often experience symptoms such as muscle weakness, myopathy, and myalgia, contributing to higher CPK levels. In severe cases, elevated CPK serves as an important diagnostic marker for muscle-related complications in hypothyroidism.<sup>11</sup>

Beyond serving as a marker of muscle injury, elevated creatine phosphokinase (CPK) levels have been strongly linked to cardiovascular risk. Studies have shown that increased CPK levels, particularly CPK-MB—an isoenzyme primarily found in cardiac muscle—are associated with myocardial injury and a greater likelihood of cardiovascular events. This association is especially concerning in hypothyroid patients, as elevated CPK levels may signal ongoing cardiac or muscle damage, potentially contributing to the progression of cardiovascular disease. Therefore, monitoring CPK levels in newly diagnosed hypothyroid patients is essential for assessing and managing their cardiovascular risk effectively.<sup>11</sup> The connection between hypothyroidism, elevated CPK levels, and increased cardiovascular risk highlights the importance of early diagnosis and timely management of thyroid dysfunction, particularly in newly diagnosed patients. This association is driven by various physiological mechanisms, including disruptions in lipid metabolism, endothelial dysfunction, and muscle damage. Elevated CPK levels in hypothyroid individuals may serve as an early indicator of muscular and cardiac stress, providing crucial insight into the risk of developing cardiovascular complications.<sup>12</sup> By regularly monitoring thyroid function and CPK levels, healthcare providers can take a more comprehensive approach to evaluating cardiovascular risk in hypothyroid patients. This proactive strategy enables better prevention and management of cardiovascular complications associated with thyroid dysfunction. Hypothyroidism is known to reduce cardiac output, increase systemic vascular resistance, decrease arterial compliance, and contribute to atherosclerosis. Previous research has established a strong link between hypothyroidism and cardiovascular disease, emphasizing the need for further investigation into cardiovascular risk in these patients.<sup>8,13</sup>



In India, where both hypothyroidism and cardiovascular disease are on the rise, understanding the link between these conditions is crucial. With the increasing prevalence of thyroid disorders, recognizing the cardiovascular risks associated with hypothyroidism and elevated CPK levels is essential. Early intervention through thyroid hormone replacement therapy and routine CPK monitoring can help mitigate cardiovascular complications and improve patient outcomes. Elevated CPK levels in newly diagnosed hypothyroid patients serve as a key indicator of both muscle and cardiovascular dysfunction. The relationship between hypothyroidism, elevated CPK, and cardiovascular risk is complex, involving disruptions in lipid metabolism, vascular function, and muscle health. Given the high burden of these conditions in India, healthcare providers must proactively identify and manage these risks. By regularly assessing thyroid function and CPK levels, clinicians can enhance cardiovascular risk evaluation in hypothyroid patients, leading to better long-term health outcomes. Present study aimed to investigate the occurrence of elevated CPK levels and its association with cardiovascular risk in newly diagnosed hypothyroid patients.

#### Material & Method:

The study was conducted at Aarupadai Veedu Medical College and Hospital, Puducherry, as a cross-sectional study over 18 months. Participants were recruited from the General Medicine OPD, IPD, and Master Health Check-up Clinic. The study included newly diagnosed hypothyroid patients (TSH >10 mIU/L and free T4 <0.8 ng/dL) aged 18 years and above who provided informed consent. Patients with a previous diagnosis of hypothyroidism, those on thyroid hormone therapy, individuals with a history of heart disease, pregnancy, lactation, recent surgery, strenuous exercise, or those using statins or fibrates were excluded. The sample size was calculated as 93 based on a study by Udovicic M et al., with an expected cardiovascular risk prevalence of 42%, and for convenience, 95 participants were included using a convenience sampling technique.

After obtaining Institutional Review Committee (IRC) and ethics committee approval, a detailed history, demographic data, clinical assessment, and laboratory investigations (FT3, FT4, TSH) were recorded. Informed consent was obtained in the patient's regional language.

Additional laboratory tests, including CBC, LFT, RFT, lipid profile, and CPK levels, were performed. Participants were categorized into two groups: those with elevated CPK levels and those without. Cardiovascular risk was assessed using the PROCAM score, and findings were statistically analyzed using SPSS software.

The independent variable was elevated CPK levels in hypothyroidism, while the outcome variable was cardiovascular risk. The study aimed to determine whether elevated CPK levels in newly diagnosed hypothyroid patients could serve as an early indicator of cardiovascular risk. Ethical considerations included minimal risk from blood sample collection, with the potential benefit of improving the understanding of CPK elevation in hypothyroidism and its link to cardiovascular risk.

**Statistical analysis** involved descriptive statistics such as mean, standard deviation, frequency, and percentage. The prevalence of elevated CPK levels was calculated with a 95% confidence interval. Logistic regression analysis was used to assess the association between CPK elevation and cardiovascular risk, with odds ratios (OR) and confidence intervals (CI) calculated. A p-value <0.05 was considered statistically significant. Subgroup analyses explored variations in association by age, sex, and thyroid function levels. ROC curve analysis was performed to evaluate the diagnostic value of CPK elevation for cardiovascular risk, with all statistical analyses conducted using SPSS v23.0.

**Result:** Present study included total of 100 patients fulfilling inclusion criteria with mean age of 43.2±14.7yrs.

		Count	N %
Gender	Female	68	68.0%
	Male	32	32.0%
Smoker	No	74	74.0%
	Yes	26	26.0%
Diabetic	No	65	65.0%
	Yes	35	35.0%



Among them 32% were male patients and 68% were female patients, with female preponderance in the study.

Table 2: Showing mean level of parameters

	Mean	SD
FT3	2.165	.514
FT4	.512	.273
TSH	13.627	9.735
LDL	109.9	35.4
HDL	47.7	13.2
Triglycerides	142.5	46.5
SBP	125.3	13.4
PROCAM score	29.4	18.5

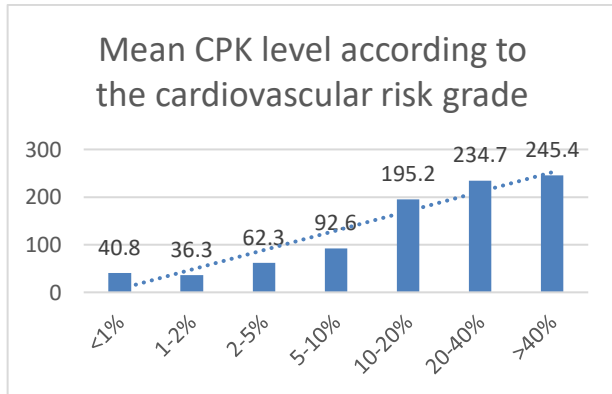


Figure 1: Mean CPK level according to the cardiovascular risk grade

Table 3: Pearson's correlation of serum CPK level with PROCAM scores and cardiovascular risk

Correlations		Serum CPK
PROCAM score	r	.742**
	p-value	.000
Cardiovascular risk	r	.768**
	p-value	.000

There is significant strong positive correlation between the PROCAM score with serum CPK levels ( $r=0.742$ ,  $p<0.01^*$ ). There is significant strong positive correlation between the cardiovascular risk with serum CPK levels ( $r=0.768$ ,  $p<0.01^*$ )

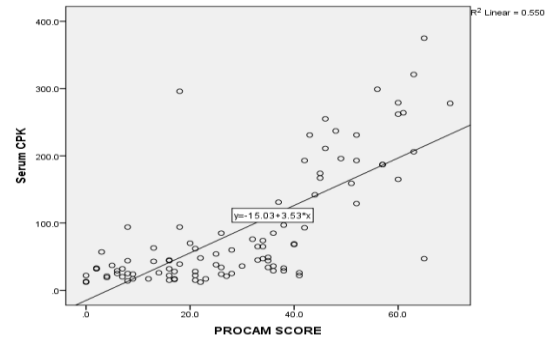


Figure 2: Pearson's correlation of serum CPK level with PROCAM scores

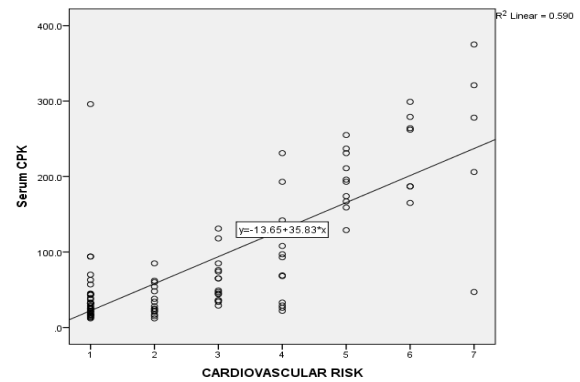


Figure 3: Pearson's correlation of serum CPK level with cardiovascular risk

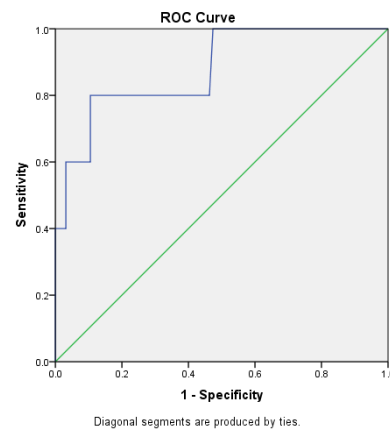


Figure 4: ROC Curve



Area Under the Curve Serum CPK				
Area	Std. Error	Asymptotic Sig. <sup>b</sup>	Asymptotic 95% Confidence Interval	
			Lower Bound	Upper Bound
.879	.082	.004	.719	1.000

The ROC curve showing the area under curve of 0.879 of CPK with PROCAM score.

**Discussion:** Present study included total of 100 patients fulfilling inclusion criteria with mean age of  $43.2 \pm 14.7$  yrs. Among them 32% were male patients and 68% were female patients, with female preponderance in the study. Among the patients 26% were smokers, 35% were diabetic.

In study by Pancholi B et al., among 55 cases 66% were male and 36% were female patients with female preponderance in their study with mean age of 45.32 yrs.<sup>14</sup>

The mean PROCAM score was found to be  $29.4 \pm 18.5$ . Among the patients, majority presented with <1% in 36%, 15% with 1-2 and 2-5%, 12% with 5-10%, 10% with 10-20%, 7% showing 20-40% and 5% with >40% cardiovascular risk. There is significant strong positive correlation between the PROCAM score with serum CPK levels ( $r=0.742$ ,  $p<0.01^*$ ) There is significant strong positive correlation between the cardiovascular risk with serum CPK levels ( $r=0.768$ ,  $p<0.01^*$ )

In study by Assmann G et al., the PROCAM showed a significant association with the dyslipidemia, diabetes mellitus, premature myocardial infarction. The ROC curve showing the 82.4% sensitivity and 82.9% specificity.<sup>15</sup>

Another study by Vanangamudi A et al., CK and LDH showed a positive correlation with TSH, and regression analysis identified a linear relationship between TSH and these markers among cases. The findings suggest that hypothyroidism significantly elevates CK and LDH activity, with CK serving as a more reliable biochemical marker for assessing muscle damage in hypothyroidism.<sup>16</sup>

Bhuce P et al., Results revealed a highly significant association between cardiac markers and TSH levels in Groups 1 and 3, while Groups 2 and 4 showed a significant correlation. The findings suggest that elevated TSH levels in SCH may lead to a notable increase in cardiac markers compared to euthyroid individuals.”<sup>17</sup> “Hypothyroidism is increasingly prevalent among individuals with chronic cardiac disease, and serum triglycerides, LDL, and HDL levels were significantly elevated in patients with coronary heart disease (CHD).”<sup>14</sup>

.Both subclinical (SCH) and clinical hypothyroidism (CH) influence target organs by altering morphology and function, while impaired blood and oxygen supply caused by accelerated atherosclerosis exacerbates these effects. The heightened risk of atherosclerosis in SCH and CH can be attributed to factors such as dyslipidemia, diastolic hypertension, arterial stiffness, endothelial dysfunction, and altered coagulation. Atherosclerotic plaque instability in hypothyroidism is linked to excessive innate immune activity, with increased macrophages, elevated NF $\kappa$ B, TNF- $\alpha$ , and MMP-9 levels, and reduced interstitial collagen creating an inflammatory environment that promotes plaque rupture. Levothyroxine (LT4) therapy restores biochemical euthyroidism, mitigating these risks. However, excessive LT4 in postmenopausal women and elderly patients with vascular comorbidities may lead to atrial rhythm disorders and osteoporosis, underscoring the importance of maintaining TSH levels within the reference range. This review highlights the interplay between SCH, CH, atherosclerosis, and LT4 therapy, focusing on its role in managing cardiovascular risks and restoring metabolic balance.”<sup>18</sup>

### Conclusion:

This study establishes a strong correlation between elevated CPK levels and increased cardiovascular risk in newly diagnosed hypothyroid patients. Among the 100 participants, the majority were female (68%), with a mean age of  $43.2 \pm 14.7$  years. Common cardiovascular risk factors included smoking (26%) and diabetes (35%). The mean CPK level was 88.8, with a median of 46.0, showing variability among patients. A significant correlation was found between elevated serum CPK levels and cardiovascular risk ( $r=0.768$ ,  $p<0.01$ ) as well as the PROCAM score ( $r=0.742$ ,  $p<0.01$ ), suggesting



CPK as a potential biomarker for cardiovascular risk assessment. Cardiovascular risk distribution revealed that 36% had a risk of <1%, while fewer patients fell into higher risk groups, with a clear trend of increasing CPK levels associated with greater cardiovascular risk ( $p < 0.05$ ). These findings highlight the importance of routine CPK monitoring in newly diagnosed hypothyroid patients for early detection and management of cardiovascular complications.

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