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# ESTIMATION OF CREATINE KINASE AND SERUM CREATININE LEVELS IN HYPOTHYROIDISM

Biochemistry

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## ABSTRACT

**Background:** Hypothyroidism is the most common endocrine disorders. Musculoskeletal and renal dysfunctions are often observed in cases of hypothyroidism anytime during the disease process.

**Aims & Objectives:** To determine the influence of thyroid hormones on creatine kinase (CK) activity and serum creatinine levels in hypothyroid patients and to determine the extent of musculoskeletal and renal involvement.

**Materials and Methods:** Serum T3 , T4 , TSH, Total CK activity and S. Creatinine levels were estimated.

**Results and Conclusion:** The rise in total CK activity in hypothyroidism can be either due to increased leakage from muscles, increased turnover of muscle proteins or can be due to decreased clearance from the circulation. Increased serum creatinine level, decreased GFR and decline in creatinine clearance were obvious in overt hypothyroidism. The elevation in serum creatinine levels in hypothyroidism can be due to skeletal muscle dysfunction with associated renal involvement.

## KEYWORDS

Creatinine, creatine kinase, hypothyroidism, TSH.

## INTRODUCTION

The thyroid gland is one of the largest endocrine gland is associated with a number of metabolic functions[1]. It is a commonest endocrine disorder all over the world.[2] Hypothyroidism is more common in women and has a total prevalence of 1% to 2%.[3] And increases with age.[4]

Mainly two hormones, thyroxin(3,5,3' 5'-L-tetraiodothyronine) and (3,5,3'-L-triiodothyronine) are secreted by thyroid gland, commonly known as $T_3$ and $T_4$ respectively[5]. Release of both these hormones is controlled by the action of thyroid stimulating hormone, which is secreted from anterior pituitary. The pathological conditions associated with thyroid gland dysfunction are hypothyroidism and hyperthyroidism. Now Hypothyroidism is a condition that arises due to the deficiency in the thyroid hormone, its action and secretion.[6] Hypothyroidism is the commonest endocrine disorder all over the world.[6]

Mainly women are found to be affected by this disorder most profoundly as compared to men, and can affect both male and female as the age increases.[6] Iodine deficiency disorder is recognized as a major public health problem in india. unlike other micronutrient deficiencies, IDD is due to deficiency of iodine in water , soil and foodstuffs, and affects all socioeconomic group living in defined geographic areas. Of the total 19 districts of haryana, india, 9 were surveyed: 8 were found to be endemic for IDD. Given the severity of iodine deficiency as a public health problem in haryana , the government banned the sale of non-iodized salt for human consumption in 1986. Hypothyroidism causes reduced metabolic function in the body such as decreased protein turnover, impaired carbohydrate metabolism and others.[8]

Myopathy may be sole clinical manifestation of hypothyroidism in the some cases with rise in serum creatine kinase (CK) activity and rise in lactate dehydrogenase and aldolase.[9] Skeletal muscle may be major source of increased plasma creatine kinase (CK) level in the subjects of hypothyroidism. Total CK activity is considered to be a sensitive and good biochemical marker for diagnosis of neuromuscular diseases.[10]. The thyroid hormones are very essential for proper growth and development of kidney and for the maintenance of water and electrolyte homeostasis. The kidneys play very essential role in the metabolism, elimination and also synthesis of thyroid hormones.[11]

Thyroid dysfunction affects the renal function by affecting the renal blood flow ,GFR, electrolyte homeostasis, Tubular function electrolyte pump function and kidney structure .The most common kidney derangement associated with hypothyroidism include the level of creatinine. Creatine is responsible for the production of creatinine by non-enzymatic irreversible dehydration. Creatinine is synthesized in the liver and kidney that passes into the circulation.[12]

## Materials And Methods

**Study design:** Hospital based cross-sectional study was done for 3 year from 2015 to 2018.

**Study population:** The hypothyroid patients from hospital laboratory of MM institute of medical sciences and research , Mullana, Ambala, Haryana .

**Study participants:** 50 diagnosed hypothyroid patients coming to the hospital lab irrespective of age and sex were selected. The diagnosis of the hypothyroidism was done on the basis of hospital lab thyroid profile results.

**Inclusion criteria:** (1) Patients with hypothyroidism. (2) Either sex (male or female) of any age.

**Exclusion criteria:** (1) Renal dysfunction (2) Muscle dystrophy (3) Arthritis (4) Diabetes mellitus.

**Study tool:** The following methodology was used for analysis:

1. Serum creatine kinase estimation- By the couple enzyme IFCC method.[13]
2. Serum creatinine estimation- By the Jaffe's method.[14]

## Ethical Considration

The present study was approved by the ethics Committee of MMIMSR. The approval was on the agreement that patient anonymity must be maintained, good laboratory practice, quality control ensured, and that every finding would be treated with utmost confidentiality and for the purpose of this research only. All the work was performed according to the International Guidelines for Human Experimentation in Biomedical Research. Approval was obtained from the subjects by filling the informed consent forms which were in English as well as Vernaculars

## Data Collection And Statistical Analysis

During data collection, completed questionnaires were checked

regularly to rectify any discrepancy, logical errors or missing information. The data entry was carried out using Microsoft Excel Worksheets and the analyzed using appropriate statistical tests (e.g. Mean, Standard deviation, Sig. (2-tailed) t-test and Pearson's coefficient) using SPS software. p value of less than 0.05 was considered significant.

## Results

1) Our study showed the higher the percentage of hypothyroidism in females than males. We had 64% (32) female and 36% (18) male patients of hypothyroidism (Fig.1).

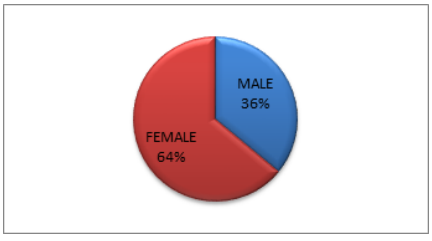


**FIG : 1 Frequency distribution in 18 male and 32 female patients with hypothyroidism.**

1) The mean and stranded deviation of various parameters of thyroid profile (T3, T4, TSH) came out to be 0.313±0.16, 2.576±1.13 and 107.97±18.98 respectively (Table.1). The serum T3, T4 levels in the patient of hypothyroid were lower the normal range and TSH level were higher than normal range. The mean and standard deviation of serum creatine kinase and serum creatinine levels in the hypothyroid patients was 471.51±99.77 and 3.05±0.52 respectively (Table.1). We found that the levels of creatine kinase and creatinine were higher than normal range in the hypothyroid patients.

**Table 1: Mean and SD of various parameters of hypothyroid patients (N=50)**

| Parameters (Normal Range) | Range Min-Max | Mean ± SD |
|---|---|---|
| T3 (0.52-1.52 ng/ml) | 0.01-0.51 | 0.313 ± 0.16 |
| T4 (4.4-11.4 mg/dl) | 0.01-4.3 | 2.576 ± 1.13 |
| TSH (0.35-5.50 µUL/ml) | 14-147 | 107.98 ± 18.98 |
| CREATINE KINASE (24 - 195 U/L) | 97-593.7 | 471.51 ± 99.77 |
| CREATININE (0.7-1.4mg dl) | 1.25-3.69 | 3.05 ± 0.52 |

3) We found the Pearson's correlation between the levels of serum creatine kinase and serum TSH of the patients with hypothyroidism. Statistical analysis showed highly significant positive correlation between serum creatine kinase levels and serum TSH levels with p value 0.0001 (Table 2, Fig.2) Serum creatinine and serum TSH in hypothyroid patients also show highly significant positive correlation with p-value 0.0001 (Table 2, Fig.3). We also found The Pearson's correlation between the levels of serum TSH and serum creatinine in both the male and female patients with hypothyroidism. There was again a highly significant positive correlation between the levels of serum TSH and serum creatinine in male subjects with p-value 0.0001 (Table 2, Fig.4), and serum TSH and serum creatine kinase also show the positive correlation in the female subjects with p-value 0.0001(Table 2, Fig.5). The correlation between the serum creatine kinase and serum creatinine was also positive with highly significant results (p= 0.0001) in both male and female hypothyroid subjects (Table 2, Fig.6).

**Table 2. Pearson's correlation of various parameters of hypothyroid patients (N=50)**

| Pairs of Parameters | p-value | Pearson's correlation |
|---|---|---|
| Serum Creatine Kinase/TSH | 0.0001* | 0.899 |
| Serum Creatinine/ TSH | 0.0001* | 0.984 |
| Creatinine Male/TSH Male | 0.0001* | 0.99 |
| Creatine Kinase/TSH in Female | 0.0001* | 0.86 |
| Serum Creatinine/ Creatine kinase | 0.0001* | 0.89 |
| *p < 0.001= highly significant | | |

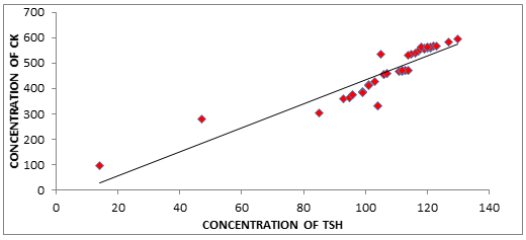


**FIG 2: Graph showing correlation between serum creatine Kinase and TSH**

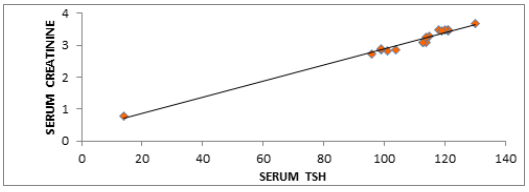


**FIG 3 : Graph showing correlation between serum creatinine and TSH**

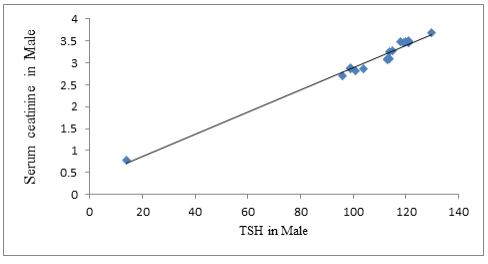


**FIG 4 : Graph showing correlation between serum creatinine and TSH in male subjects.**

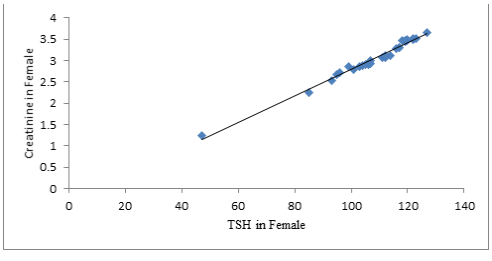


**FIG 5 : Graph showing correlation between serum creatinine and TSH in Female subjects.**

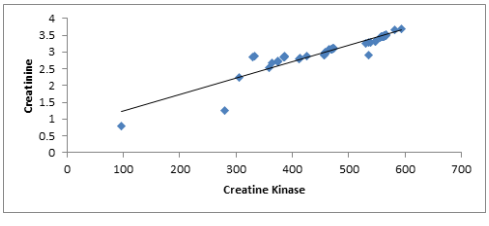


**FIG 6: Graph showing correlation between serum creatinine and creatine kinase in hypothyroidism subjects.**

## DISCUSSION

The disorder related to thyroid hormones is one of the most common endocrine disorders other than diabetes mellitus.[15] Such disorders have their association with either an increased (hyperthyroidism) or decreased activity (hypothyroidism) of the thyroid gland.[16] The chances of thyroid dysfunction are increased with age, and is mainly seen in female cases.[17] The increase in peripheral resistance can predispose to the alteration in renal hemodynamics such as reduced renal blood flow and diminution of glomerular filtration rate resulting in decreased clearance of certain substances like creatine kinase, creatinine and others in hypothyroidism.[18] Hypothyroids had increased activity of CK, due to increased CK-MM isoenzyme which indicates skeletal muscle as the major source of the increased plasma activity. And the elevation of serum creatinine levels in hypothyroidism is due to skeletal muscle dysfunction with associated increase in total serum

creatine kinase activity and also due to renal involvement.[19]The decrease in renal plasma flow and glomerular filtration rate (GFR) that accompany hypothyroidism are believed to be related to the generalized hypodynamic state of the circulatory system in hypothyroidism. Skeletal muscles may be the major source of increased plasma CK activity in hypothyroidism[20].

In our study, the levels of creatine kinase increase with increase in hypothyroidism. There are some previous studies of creatine kinase, which show a resemblance to our present study results. Similarly **Archna P et al** [21], **Rashmi Ranka et al** [22] showed that the mean values of creatine kinase (CK) levels in hyperthyroid patients were lower as compared to the hypothyroid patients. Serum creatine kinase levels thus showed an inverse relation with serum T3, T4 levels. **Khaleeli et al.**[23] also reported elevation of serum CK activities correlating with the severity of hypothyroidism. The thyroid hormones have an oxidative metabolism in muscles. The renal dysfunction in hypothyroid patients can be due to decrease in renal plasma flow and associated to the reduction in glomerular filtration rate. High serum CK concentration in hypothyroidism may be due to muscle fiber degeneration, altered muscle energy metabolism and decreased clearance of CK from circulation. **Hekimsoy Z et al.**[24] also found the highly significant positive correlation between TSH and CK activity in both overt and subclinical cases. Which showed that there was a rise in TSH levels along with serum CK activity in hypothyroidism. However, the rise in CK activity was many folds higher in overt cases as compared to subclinical cases.

In our study the creatinine levels were found to be increased in the hypothyroidism patients. We also found that a positive correlation was present between serum creatinine and serum TSH levels. Serum creatinine levels were came out to be $3.05 \pm 0.52$. Similarly, **Englund FI et al** [25], **Kreismanet al** [26] and **Tayal et al** [27] have also reported significant elevation in serum creatinine levels in hypothyroid patients, but the elevation was being more in overt hypothyroids as compared to subclinical hypothyroids. Increase in the serum creatinine level was found in all types of hypothyroids due to decreased GFR. And a significant positive correlation between eGFR and creatinine clearance in hypothyroids was noted as indicative decrease in creatinine clearance due to reduced filtration rate. In patients of hypothyroidism, eGFR is decreased. As filtration rate is decreased creatinine clearance is decreased and so there existed an increase in serum creatinine concentration in both Subclinical and overt hypothyroidism. **Saini V et al** [28] studied the patients of overt hypothyroid and of subclinical hypothyroidism. According to their study overt hypothyroid subjects showed significantly increased serum creatinine as compared to controls. And TSH showed significantly positive correlation with creatinine values.

In our study, a positive significant correlation was found between the serum creatinine kinase and serum creatinine in the hypothyroid patients. The level of creatinine increases due to rise in the level of creatine kinase in the hypothyroidism due to decreased GFR. **Mathew George et al** [29] in their study found a significant alteration in Creatine kinase, creatinine, and estimated GFR (eGFR) in hypothyroid patients, which might be due to renal and muscular damage resulting in renal failure and myopathies

In our study, a positive significant correlation was found between the age and hypothyroidism in the female cases. This indicates that the chances of hypothyroidism are more in females as compared to males. Thyroid is related to reproductive hormones in two ways. Firstly, thyroid hormone regulates metabolism & many physiological activities of the body, including reproductive gland activity. Secondly, thyroid hormones have similarities with certain metabolites of estrogen, progesterone& receptor sites for thyroid uptake, can be blocked or facilitated by estrogen &progesterone. Imbalances of thyroid hormones T3 & T4, combined with imbalances of estrogen & progesterone can produce many different consequences in the areas of mood, temperature regulation, fluid retention, energy & sleep. Some study showed a relation between age and hypothyroidism. Their study concluded that the distribution of serum TSH shifted progressively to higher concentration with age.[16] Lipson et al also concluded that the values of T3 showed a gradual decline by decades in total T3 in subjects over 60 years. Among the possible explanations for the fall in total T3 are: (a) a decline in thyroid secretion, (b) an increase in T3 turnover rate, (c) a decline in TBG and, (d) a decrease in peripheral conversion of T4 to T3.[30] It is not likely that lower serum T3 values in old age are the result of a decrease in TBG.[31]Hesch et al. confirmed in their study of older normal subjects with low total T3. A possible explanation for which might be decreased thyroidal T3 production and release. It is possible that the degradation rate of T3 increases in old age [32]. In our study serum creatinine and creatine kinase levels increased with the prevalence of hypothyroidism. Correlation between T3 and TSH was negative and correlation between TSH & serum creatinine came out to be highly significant.

## CONCLUSION

In the present study, we concluded that T3 and T4 levels decrease with increase in TSH levels in hypothyroid patients. On the other hand creatinine and creatine kinase levels increase in hypothyroid patients. We also observed that TSH levels increase with age. We can say that any change in thyroid hormone levels has influence on the function of skeletal muscles. It might be associated with decrease in renal perfusion and filtration capacity. In the hypothyroidism skeleton muscle involvement occurs before dysfunction of renal. The increase in the level of serum creatinine in hypothyroidism may be because of skeletal muscle dysfunction with associated elevation of total creatine kinase activity and partly due to renal involvement.

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