

Evaluation of serum creatinine in subclinical hypothyroidism A case – control study

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ABSTRACT

Background: Hypothyroidism is a clinical condition characterized by abnormally low thyroid hormone production. Hypothyroidism results in slowing down of metabolic processes. Subclinical hypothyroidism is associated with biochemical abnormalities including increased serum creatinine level.

Objectives: This study was designed to estimate the serum creatinine level in subclinical hypothyroidism cases and to assess the correlation of serum creatinine with fT3, fT4, TSH.

Material and methods: Study included 61 patients of subclinical hypothyroidism and 61 age, sex matched healthy controls. Venous blood was analyzed for testing creatinine and fT3, fT4, TSH levels. Statistical analysis was done using student 't' test. Pearson's correlation between the creatinine and thyroid parameters was performed to establish the relationship.

Results: The serum creatinine level was significantly elevated in subclinical hypothyroidism cases in comparison to controls. Creatinine showed significant positive correlation with TSH and negative correlation with fT3, fT4 levels.

Conclusion: Subclinical hypothyroidism is associated with elevated serum creatinine level.

Key words: fT3 (free triiodothyronine), fT4 (free tetraiodothyronine), TSH (thyroid stimulating hormone), creatinine, subclinical hypothyroidism.

INTRODUCTION

Thyroid is an endocrine gland. It produces thyroxine (T4) and tri-iodothyronine (T3) which act through receptors inside the nucleus. Thyroid stimulating hormone (TSH) secreted by thyrotrope cells of anterior pituitary plays a very important role in control of thyroid axis and serves as the most important marker of thyroid hormone action. Hypothyroidism is a clinical condition characterized by abnormally low thyroid hormone production. Primary hypothyroidism results when thyroid gland fails to produce adequate hormones. In secondary hypothyroidism the hypothalamic-pituitary–thyroid axis works inadequately¹. Hypothyroidism is one of the most common endocrine disorders in India. It affects 2-15% of population worldwide and women are more commonly affected compared to men. Most common cause is iodine deficiency and another cause is autoimmune thyroid disease characterized by elevated anti-Thyroid Peroxidase antibody². Subclinical hypothyroidism is characterized by increased TSH and normal fT3, fT4 serum levels. Subclinical hypothyroidism affects virtually every tissue in the body. This includes slowing of physical and mental activity³. Long standing hypothyroidism can cause reversible changes in the metabolic parameters such as increase in serum creatinine. Thyroid dysfunction causes remarkable changes in glomerular and tubular functions and electrolyte and water homeostasis. Hypothyroidism is accompanied by a decrease in glomerular filtration, elevation of

serum creatinine and alteration of the ability for water excretion^{3,4}. Many articles mention serum creatinine is increased in overt hypothyroidism but not in subclinical hypothyroidism. Few of the articles show that it is increased in both subclinical and overt hypothyroidism cases. Hence the aim of this study is to estimate and compare serum creatinine level in subclinical hypothyroid cases and healthy controls and to correlate serum creatinine level with TSH, fT3, fT4.

MATERIALS AND METHODS

This case control study comprises of 61 newly diagnosed subclinical hypothyroidism cases and 61 age and sex matched healthy controls, attending medicine outpatient department of HSK hospital and research centre Bagalkot. Institutional ethical committee clearance was obtained for the study. Duration of the study was from January 2015-july 2015. Patients with newly diagnosed hypothyroidism in the age group of 20 to 59 years of both gender were included. Patients with chronic kidney disease, muscular dystrophies, gout, hypertension and patient on drugs were excluded from the study. Informed written consent was obtained from all the subjects enrolled for the study and detailed history was taken. 3 ml venous blood was obtained in plain tube. fT3, fT4, TSH were estimated by using SNIBE 1000 machine and kits were supplied by Maglumi by CLIA⁵. Serum creatinine was measured using semiauto-analyser

ERBACHEM-5x and kit supplied by ERBA. Creatinine was estimated by alkaline picrate method⁶.

STATISTICS

Statistical analysis was done using student ‘t’ test for comparison of two groups and a ‘p’ value of < 0.05 was considered statistically significant. Pearson’s correlation between study variables was performed to establish the relationship.

RESULTS

This study showed significant difference in serum levels of TSH, FT3, FT4 and creatinine between the study group and control group. The levels of serum creatinine in subclinical hypothyroid cases (0.95 ± 0.21) were higher compared to euthyroid subjects (0.66 ± 0.11) which is highly significant ($p < 0.001$).

Table 1: Comparison of age in Subclinical hypothyroidism cases and controls.

Variables	Subclinical hypothyroid cases	Controls	p value
Age in years	34.08 ± 10.36	33.79 ± 9.92	0.81

Table 2: Thyroid parameters levels in subclinical cases and controls.

Thyroid parameters	Subclinical hypothyroid cases	Controls	p value
FT ₃ pg/ml	2.31 ± 0.43	2.37 ± 0.52	0.53
FT ₄ pg/ml	11.5 ± 1.55	13.87 ± 1.67	<0.001**
TSH μ IU/ml	20.95 ± 12.07	2.01 ± 0.90	<0.001**

Table 3: Serum levels of creatinine in Subclinical hypothyroidism cases expressed as mean \pm SD.

Parameter	Subclinical hypothyroid cases	Controls	p value
Serum creatinine	0.95 ± 0.21	0.66 ± 0.11	< 0.001**

Serum Creatinine showed significant positive correlation with TSH level in subclinical hypothyroid cases.

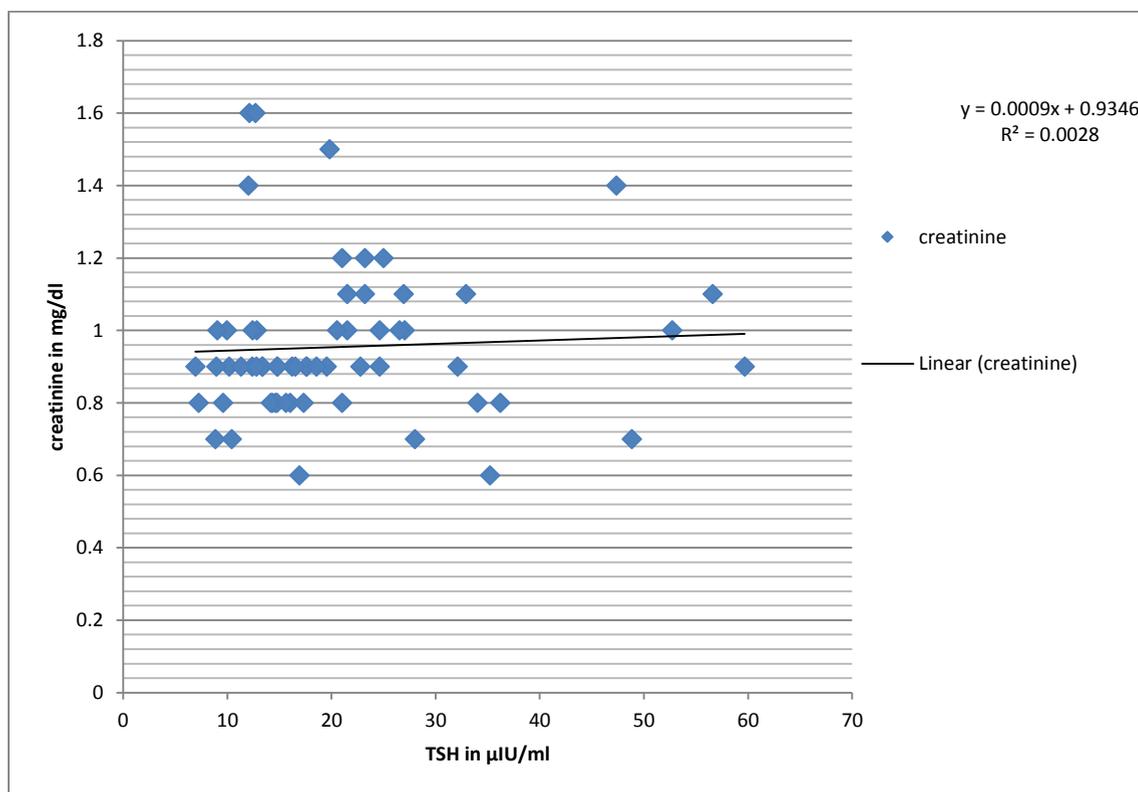


Figure 1: Positive correlation of serum creatinine with TSH.

DISCUSSION

Hypothyroidism is a clinical syndrome resulting from deficiency of thyroid hormones, leading to generalized slowing of all metabolic process. The prevalence of hypothyroidism varies in different regions of the world and is more prevalent in females⁷. Thyroid dysfunction causes significant changes in kidney function and the most common kidney derangements associated with hypothyroidism is elevation of serum creatinine levels, reduction in glomerular filtration rate and renal plasma flow. Primary subclinical hypothyroidism is associated with a reversible elevation of serum creatinine in both adults and children^{3,7}.

Our study showed that there is increased serum creatinine levels (0.95 ± 0.21) in subclinical hypothyroidism cases as compared to euthyroid controls (0.66 ± 0.11). This is in accordance with study done by Ajaykumar, showed an increase in serum creatinine with a mean of 1.11 and increase in serum uric acid with a mean of 7.35 in primary subclinical hypothyroidism cases and these metabolic parameters were found to be reversible after thyroxine replacement therapy. The increase in serum uric acid and creatinine may be either due to increased production or decreased renal clearance. GFR is believed to be due to the generalized hypodynamic circulation in hypothyroid patients⁸.

Another study conducted by Sarika Arora et al, which showed that there is significant increase in creatinine levels (0.85 ± 0.29) in overt hypothyroid subjects as compared to euthyroid subjects (0.71 ± 0.27). These changes may result in physiological effects including alterations in renal hemodynamics, decrease in GFR and hence reduced clearance of creatinine⁹.

Iglesias study on thyroid dysfunction and kidney disease shows elevation of serum creatinine levels due to decreased glomerular filtration rate and due to decreased renal plasma flow. Primary hypothyroidism is associated with a reversible elevation of serum creatinine in both adults and children³.

Study conducted by Sinisa et al, observed increase in serum creatinine in hypothyroid subjects $115 \pm 12 \mu\text{mol/L}$ which decreased after treatment to $95 \pm 14 \mu\text{mol/L}$. Decreased GFR, decreased creatinine clearance and decreased creatinine tubular secretion together with the increased release of creatinine from muscle cells explain the higher values of serum creatinine in hypothyroidism¹⁰.

CONCLUSION

Serum creatinine level is significantly higher in subclinical hypothyroid patients. So hypothyroidism should be taken into account in patients presenting with elevated serum creatinine levels. On other hand, Chronic kidney diseases cases should

also be screened for hypothyroidism. Subclinical hypothyroidism should be detected at early state and restrict its progression to overt hypothyroid state and prevent organ damages.

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