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Original Article

Serum Creatinine Level and its Relation with Thyroid Profile: a Cross-Sectional Study among Newly Diagnosed Hypothyroid Patients

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ABSTRACT

CONTEXT: *Hypothyroidism is considered one of the known global public health complications affecting human kidney function.* ***OBJECTIVE****: This study aimed to analyze the effect of hypothyroidism on serum creatinine levels and the correlation between the extent of hypothyroidism and serum creatinine levels among newly diagnosed hypothyroid subjects.* ***METHODS****: The study subjects were selected from patients undergoing thyroid evaluation in Nuclear Medicine and Allied Sciences, Rajshahi from July 2018 to June 2019. Among them 60 participants were selected, 30 were hypothyroid cases and 30 were age and sex-matched controls with normal thyroid profiles (euthyroid). Recently diagnosed and untreated cases were selected. A purposive sampling technique was used to select each study subject. The blood sample was collected from non-fasting subjects. T3, T4, and TSH were assayed by RIA and IRMA techniques. Serum creatinine was measured by Jaffe's method in an alkaline medium on a semi-auto analyzer. The test of significance was calculated by using an unpaired student-t test. A p-value less than 0.05 was considered significant.* ***RESULTS****: In the present study we found the mean value of serum creatinine was significantly higher in hypothyroid patients as compared to euthyroid controls. And also there was a strong positive correlation was seen between TSH and creatinine in the hypothyroid group. Creatinine had a positive correlation with T4 ($p<0.01$) but showed a negative correlation with T3 level in hypothyroidism.* ***CONCLUSION****: This recommends that as hypothyroidism patients have significant changes in serum creatinine level it can be suggested that patients with unexplained abnormal renal function should be screened for hypothyroidism.*

Keywords: Hypothyroidism, serum creatinine, T4, T3, TSH

INTRODUCTION

Hypothyroidism is a common endocrine disorder. The number of hypothyroid patients in North Bengal is relatively high. It is endemic in some areas like Sirajganj, Bogura, Jypurhat, and Gaibandha.[1] Hypothyroidism is a clinical entity resulting from the deficiency of thyroid hormones or from impaired activity.[2] There are several aspects of the relationship between the thyroid gland and kidneys. Thyroid hormones are known to be involved in the development and function of the kidneys and conversely, kidney function can affect the concentration and metabolism of thyroid hormones.[3] The thyroid hormones play a vital role in various metabolic pathways within the human biochemical reactions and any alteration in the amount of serum thyroid hormones, directly cause metabolic disorders, in various organs and modify the normal metabolic pathways of various organs, including the kidney.[4] Long-standing hypothyroidism can cause significant changes

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in renal function such as a decrease in sodium reabsorption in the proximal tubule, impairment in the concentrating and diluting capacities of the distal tubules, a decrease in the urinary urate excretion and a decrease in the renal blood flow and glomerular filtration rate (GFR). In hypothyroidism, physiological effects include changes in water and electrolyte metabolism, alterations of renal hemodynamics, lowered renal blood flow, renal plasma flow, glomerular filtration rate (GFR), and single nephron GFR.[5] Serious hypothyroidism can also be accompanied by morphologic changes in the glomeruli such as thickening of the glomerular basement membrane, as well as increased mesangial matrix, thickening of the tubular basement membrane, and cytoplasmic inclusions in renal tubular epithelial cells.[6] Very few studies have reported the effect of hypothyroidism on renal function tests especially creatinine.[7] The concentration of serum creatinine is also distorted in hypothyroidism resulting in elevated serum creatinine concentration. There is a marked increase in creatinine as a result of decreased creatinine clearance due to decreased filtration rate and increased production of serum creatinine. In SCH (Subclinical hypothyroidism) when compared with the euthyroid group, serum creatinine was considerably raised as compared to standard. Serum creatinine values were approximately 35% higher in the hypothyroid state. Primary hypothyroidism is associated with reversible elevation of serum creatinine in both adults and children. It was observed in 55% of adults.[8] The present study was therefore designed to determine the effects of hypothyroidism on serum creatinine levels.

MATERIALS AND METHODS

It was a cross-sectional analytical type study. The study subjects were selected from patients undergoing thyroid evaluation in Nuclear Medicine and Allied Sciences, Rajshahi from July 2018 to June 2019. Among them 60 participants were selected, 30 were hypothyroid cases and 30 were age and sex-matched controls with normal thyroid profiles (euthyroid). Recently diagnosed and untreated cases were selected. A purposive sampling technique was used to select each study subject. Patients with newly diagnosed thyroid disorders in the age group of 20 to 60 years of both genders were included. Those having normal T3, T4, and TSH levels were categorized as euthyroid. Those having low T3, T4, and high TSH levels were categorized as hypothyroid with respect to the reference range. The protocol of the study was approved by the Ethical Review Committee (ERC) and Institutional Review Board (IRB) of Rajshahi Medical College. All the subjects were free from Diabetes, Hypertension, Chronic liver and renal disease, Alcoholism, and Smoking. Before recruitment, the aim, benefit, and procedure of the study were explained, and informed written consent was taken from each study subject. Thorough physical examinations of all subjects were done. The blood sample was collected from non-fasting subjects. T3, T4, and TSH were assayed by RIA and IRMA techniques. Serum creatinine was measured by Jaffe's method in an alkaline medium on semi auto analyzer. Data were analyzed by computer using the SPSS software program. The test of significance was calculated by using an unpaired student-t test. A p-value less than 0.05 was considered significant. The Pearson correlation was applied to check whether T3, T4 and TSH were correlated with renal function marker creatinine.

RESULTS

A total number of 60 subjects participated in this study. Among them 30 hypothyroidism and 30 euthyroidism were taken in this study.

Table I: Distribution of age among the respondents

Age group	Hypothyroidism (Cases)		Euthyroidism (Control)	
	No	%	No	%
20-30 years	7	23.3	6	20.0
31-40 years	14	46.7	13	43.73
Above 40 years	9	30.0	11	36.7
Total	30	100	30	100

According to Table I study population were divided into three different age groups, 20-30 years, 31-40 years and above 40 years. Among the study population 31-40 years group constituted the highest number followed by above 40 years age group in both hypothyroidism and euthyroidism. In both hypothyroidism and euthyroidism 20-30 years was the smallest group.

Table II: Distribution of gender among the respondents

Gender	Hypothyroidism (Cases)		Euthyroidism (Control)	
	No	%	No	%
Male	9	30	8	26.7
Female	21	70	22	73.3
Total	30	100	30	100

Table II represented that out of 30 Hypothyroidism, 70% were female and 30% were male. Similar results were also obtained from control group that female were more than male in case group.

Table III: Distribution of individuals basic health parameters

Variables	Hypothyroidism (n-30) (mean±SD)	Euthyroidism (n=30) (mean±SD)	P-value
Age	37.47±9.97	38.9±10.00	0.5813^{NS}
Weight	61.33±12.20	61.10±10.8	0.2823^{NS}
Height	62.00±2.94	61.6±2.42	0.5667^{NS}
BMI	25.80±4.34	25.00±3.70	0.4534^{NS}

* NS: Not Significant, SD: Standard deviation * The test of significance was calculated using unpaired-t test.

Table III showed the distribution of different health parameters, age in years, weight in kg, height in inch, and BMI in kg/m^2. Values of basic characteristics were expressed as mean±SD. Statistical analysis showed that there is no statistical differences in age, weight, height and BMI between two groups hypothyroidism and euthyroidism. The value of mean±SD of weight and BMI are little bit higher in hypothyroidism patients than euthyroidism.

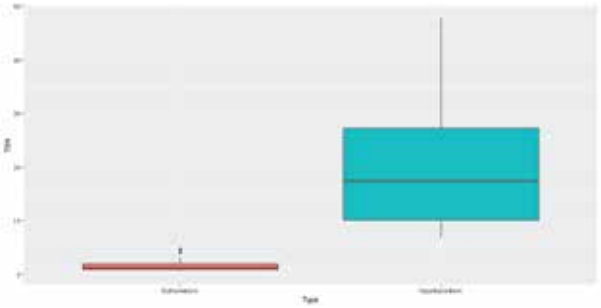

Figure 1: Box Plot of TSH between Hypothyroidism and Euthyroidism.

From figure 1, it is observed that lowest value, first quartile, third quartile and highest value of TSH were highly differed in hypothyroidism and euthyroidism group, while the median value of TSH in hypothyroidism was higher than euthyroidism group.

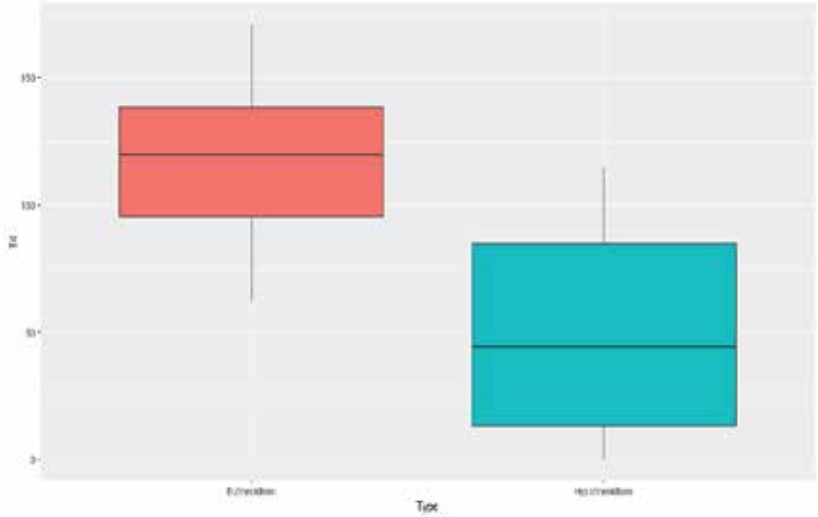

Figure 2: Box Plot of T4 between Hypothyroidism and Euthyroidism.

Figure 2, represented that lowest value, first quartile, third quartile and highest value of T_4 were highly differed in hypothyroidism and euthyroidism group and median value of T_4 in hypothyroidism is lower than euthyroidism group.

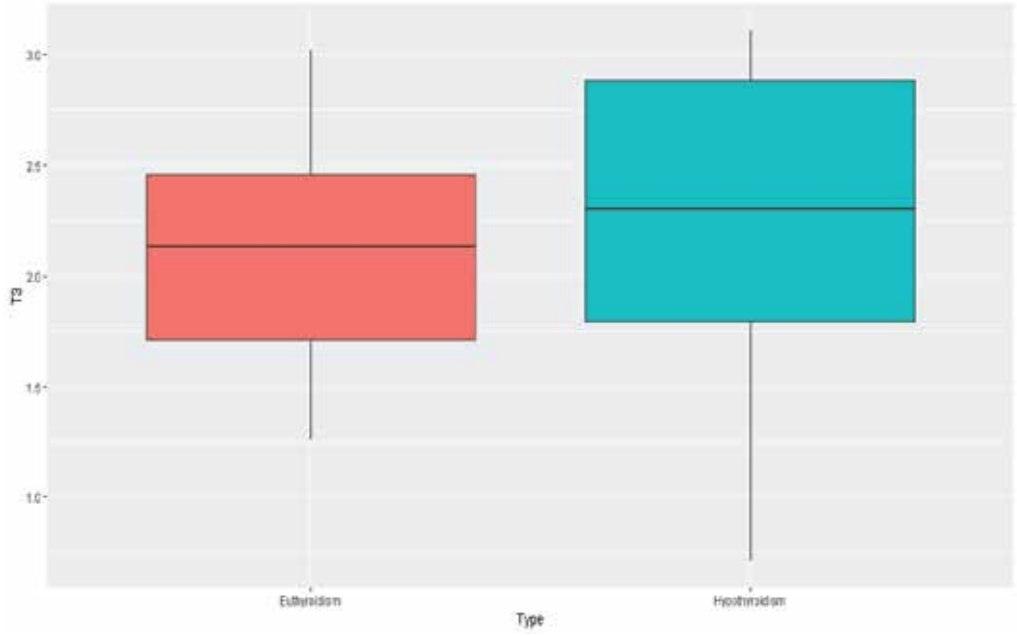

Figure 3: Box Plot of T_3 between Hypothyroidism and Euthyroidism.

From figure 3 we found that lowest value, first quartile, third quartile and highest value of T_3 were almost same in hypothyroidism and euthyroidism group. Median value of T_3 is slightly higher in hypothyroidism than euthyroidism group.

Table V: Distribution of the Thyroid Stimulating Hormone (TSH), Thyroxine (T_4) and Tri-iodothyronine (T_3) between Hypothyroidism and Euthyroidism.

Parameters	Hypothyroidism (n=30) (mean±SD)	Euthyroidism (n=30) (mean±SD)	P-value
TSH(µIU/ml)	20.27±11.7	1.50±1.05	$<0.001^S$
T_4(nmol/L)	48.96±38.0	118.57±30.1	$<0.001^S$
T_3 (nmol/L)	2.25±0.693	2.10±0.486	0.3284^{NS}

*S: Significant and NS: Not Significant.
* The test of significance was calculated using unpaired-t test.

Table V showed that the value of mean±SD of TSH, T_4 and T_3 in hypothyroidism and euthyroidism. The (mean±SD) of serum TSH level in hypothyroidism 20.27±11.7 was higher than that of euthyroidism 1.50±1.05 (µIU/ml), which was statistically significant. The value of mean±SD of serum T_4 level in hypothyroidism 48.96±38.0 was lower than that of euthyroidism 118.57±30.1nmol/L, which was also statistically significant. Again, the value of mean±SD of serum T_3 level in hypothyroidism 2.25±0.693 was slightly higher than that of euthyroidism 2.10±0.486 nmol/L, which was not statistically significant.

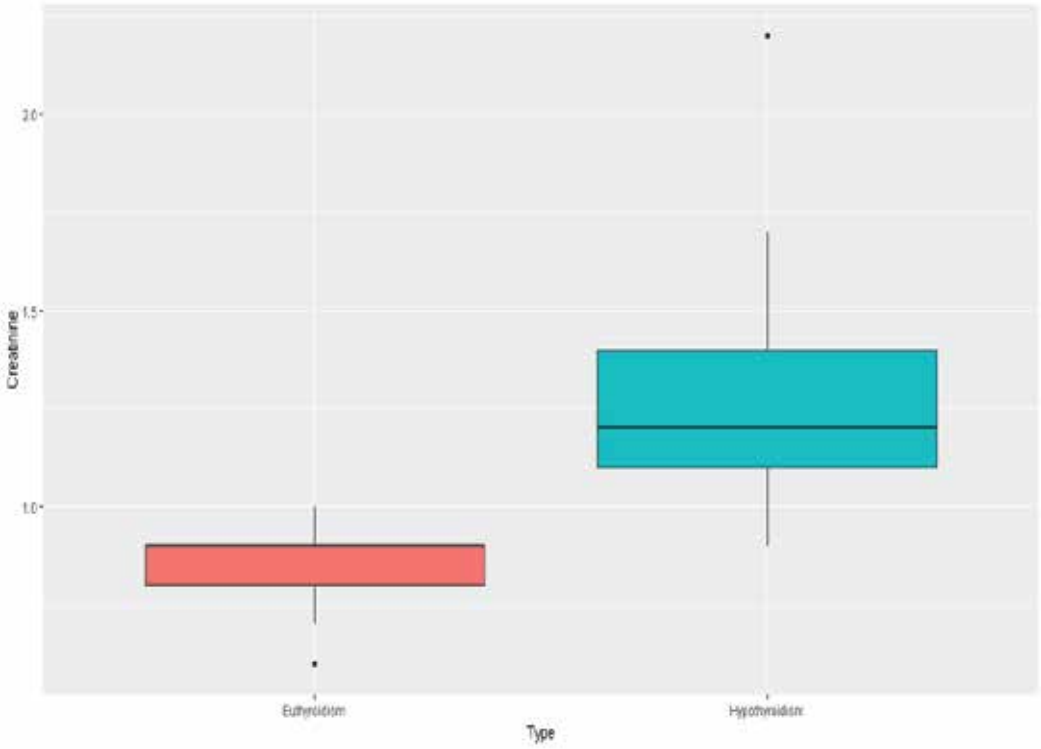

Figure 4: Box plot of Creatinine level between Hypothyroidism and Euthyroidism.

From figure 4 we observed that lowest value, first quartile, third quartile and highest value of creatinine has differed highly between hypothyroidism and euthyroidism group. Median value of creatinine is higher in hypothyroidism than euthyroidism group.

Table VI: Correlation between age and creatinine level of Hypothyroidism patients

	Age	Creatinine level
Age	1	0.341[s]
Creatinine level	0.341[s]	1
Total	30	30

* s: significant
* The test of significance was calculated using correlation coefficient test.

The value of correlation coefficient between age and creatinine level of Hypothyroidism patients was 0.341 (Table VI), which indicated that there was a significant positive observed correlation between age and Creatinine level, i.e. with the increase of age, creatinine level will also increase.

Table VII: Distribution of the Creatinine between Hypothyroidism and Euthyroidism.

Biochemical parameter	Hypothyroidism (n=30) (mean±SD)	Euthyroidism(n=30) (mean±SD)	P-value
Creatinine (mg/dl)	1.27±0.273	0.85±0.12	<0.001[S]

*S: Significant and NS: Not Significant.
* The test of significance was calculated using unpaired-t test.

The value of mean ± SD of serum creatinine in hypothyroidism and euthyroidism is 1.27±0.273 and 0.85±0.12 mg/dl respectively. The P-value indicated that there was a statistical significant difference of creatinine between hypothyroidism and euthyroidism group (Table VII).

Table VIII: Correlation between age and creatinine level of Euthyroidism

	Age	Creatinine level
Age	1	0.192[ns]
Creatinine level	0.192[ns]	1
Total	30	30

The value of mean ± SD of serum creatinine in hypothyroidism and euthyroidism was not statistical significant difference of creatinine between hypothyroidism and euthyroidism group (Table VIII).

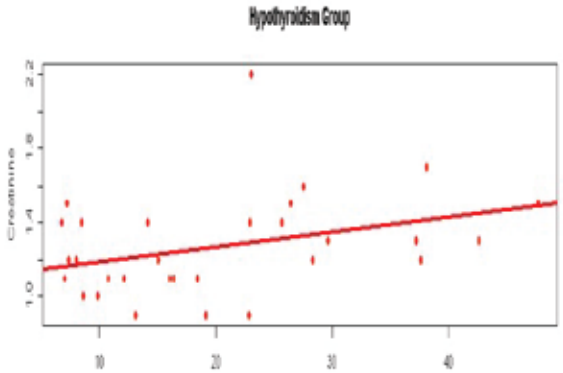

Figure 5: Scatter plot of TSH and Creatinine in hypothyroid group.

Figure 5 showed that there is a strong positive correlation between TSH and creatinine in hypothyroid group.This means that if the value of TSH level is increased, serum creatinine level is also increased & vice-versa.

DISCUSSION

Thyroid hormone is a central regulator of body functions that is metabolism and hemodynamics. The purpose of the present study was to evaluate the effect of hypothyroidism on parameters of renal function that is serum creatinine, compare it with euthyroid subjects and also to study the correlation of TSH with creatinine.

According to Table I study population were divided into three different age groups, 20-30 years, 31-40 years and above 40 years. Among the study population 31-40 years group constituted the highest number 14(46.7%) and 13(43.73%) followed by above 40 years age group 9(30%) and 11(36.7%) in both hypothyroidism and euthyroidism respectively. In both hypothyroidism and euthyroidism 20-30 years was the smallest group that is 7(23.3%) and 6(20%) respectively.

Distribution of study groups according to their gender the percentage of females was more than the percentage of males (Table II). The results of this study were similar to a study who recorded hypothyroidism was more frequent in females.[1]

In the present study there was a highly significant difference of TSH level ($P<0.001$) between cases and controls group. There was also a highly significant difference in T_4 level ($P<0.001$) due to the two same categoral. The mean value of T_3 is slightly higher in hypothyroidism than euthyroidism which is not statistically significant (Table IV).

Table V and figure 4 represent value of serum creatinine between two groups. In this study there was a highly significant increase in serum creatinine in hypothyroidism when compared to euthyroidism. But this value is within the normal reference range. The result of this study was agreed with[1,3,7,9-19] found significant increase in serum creatinine level in hypothyroidism than euthyroidism. There was also a very strong positive correlation was found between TSH and cretinine in hypothyroidism which shown in (Figure 5). Serum creatinie concentration increases in hypothyroid patients due to reduction of glomerular filtration rate because of hemodynamic changes in severe hypothyroidism.[9] In a study it was found that mean level of serum creatinine is slightly higher in hypothyroidism than euthyroidism but this value was non-significant.[20] Her selected case group was diagnosed with suffering from hypothyroidism, who might be on the L-thyroxin replacement therapy this is the possible cause of non-significant finding.

Thyroid dysfunction causes remarkable changes in glomerular and tubular function and electrolyte and water homeostasis. Thyroid hormone leads to increase in nitric oxide levels in blood vessel which causes vasodilatation resulting in increased GFR, however in hypothyroidism there is a decrease level of nitric oxide in blood vessels which increases systemic vascular resistance thus reducing renal blood flow & in turn decreases GFR thus resulting increase blood creatinine level.[18]

There was a significant but weak correlation was found between age and creatinine in hypothyroidism patient (Table VII) but non-significant in Euthyroidism (Table VIII).

One of the strength of this study was that we have included newly diagnosed and untreated both female and male patients in our study.

This type of patient selection can predict relatively accurate finding of our parameters.

One of the weaknesses of this study was that we have done cross sectional study on smaller sample size and did not supplement L-thyroxin therapy. So longitudinal study on larger sample size should be done and effect of L-thyroxin replacement therapy should be monitor to confirm our finding. Moreover, many other clinical parameters such as creatinine clearance test, serum urea level could not be collected for laboratory records which could have been correlated.

The overall results of our study presented that serum creatinine level significantly increased in cases of newly diagnosed hypothyroid patients. So a regular periodic screening needed to establish the relation needed to establish this relationship.

CONCLUSION

From the findings of the present study, it can be demonstrated that hypothyroidism was associated with significant changes in serum creatinine. There was a significant difference in plasma creatinine concentration between hypothyroid patients and euthyroid individuals. There was also a very strong positive correlation was found between TSH and creatinine. Finally, it can be concluded that hypothyroidism patients should be regularly screened and check renal serum creatinine.

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