

ORIGINAL RESEARCH

To evaluate the effect of hypothyroidism on the renal functions of the body

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Abstract

Introduction: The interactions between thyroid gland and renal functions are known for years. Thyroid dysfunction can affect renal physiology and development, and on the other hand, kidney disorders can influence thyroid function. Hence; the present study was done to evaluate the effect of hypothyroidism on the renal functions of the body

Material and Methods: This one-year observational prospective study will be conducted in the Postgraduate Department of Internal Medicine, Government Medical College and Hospital, Jammu with effect from November, 2019 to October, 2020. Recording of detailed history including history of cardiovascular disease, diabetes mellitus, hypertension, surgery, or any drug intake and family history of renal, muscular, liver disorders. Measurement of anthropometric indices like weight, height, BMI. Recording of vital signs. Blood investigations including serum uric acid, serum creatinine, fT3, fT4 and TSH. The statistical analysis was done using (SPSS 22.00 for windows; SPSS inc, Chicago, USA).

Results: In both the groups, females were comparatively more as compared to males. When mean creatinine and Uric Acid (mg/dl) was compared statistically among case and control group, it was found to be statistically significant as $p < 0.05$. Positive significant correlation was found between TSH and creatinine ($r = 0.54$, $p < 0.01$) and and uric acid ($r = 0.61$, $p < 0.01$).

Conclusion: This study confirms that hypothyroidism is associated with a consistent elevation in the serum creatinine and uric acid levels. Therefore, we would suggest assessment of thyroid function in patients presenting with deranged renal function.

Keywords: Glomerular filtration rate (GFR), Hypothyroidism, Thyroid stimulating hormone (TSH).

Introduction

In 1656, it was believed in Western world that the major role of the thyroid gland was to lubricate the trachea¹. In females, the gland was assumed to have an ornamental purpose. Later in the same year, the anatomist Thomas Wharton identified the thyroid gland².

Thyroid hormones are essential for normal growth, tissue differentiation, general development and metabolism. Thyroid stimulating hormone (TSH) secreted by thyrotrope cells of anterior pituitary plays a very important role in the control of thyroid axis and serves as the most important marker of thyroid hormone action. TSH is a very sensitive and specific parameter for determining thyroid function and is important in early detection or exclusion of thyroid disorders³.

The interactions between thyroid gland and renal functions are known for years. Thyroid dysfunction can affect renal physiology and development, and on the other hand, kidney disorders can influence thyroid function.

Hypothyroidism, in turn, slows down all metabolic processes. In hypothyroidism, due to decreased cardiac output, increased peripheral vascular resistance, vasoconstriction in the renal vasculature, reduced renal response to vasodilators, and decreased expression of renal vasodilators, such as vascular endothelial growth factor and insulin like growth factor 1, renal blood flow (RBF) is reduced. Glomerular filtration rate (GFR) also diminishes due to reduced sensitivity to beta-adrenergic stimuli and decreased renin secretion.

Decreasing GFR and RBF along with rhabdomyolysis and myopathy induced by hypothyroidism increase serum creatinine. Hypothyroidism is a clinical syndrome that is divided into overt and subclinical forms⁴.

Hence; the present study was done to evaluate the effect of hypothyroidism on the renal functions of the body.

Material and Methods

This one-year observational prospective study was conducted in the Postgraduate Department of Internal Medicine, Government Medical College and Hospital, Jammu with effect from November 2019 to October, 2020. The participants in this study were either known hypothyroid not on treatment for at least 3 months or newly diagnosed hypothyroid individuals not started on thyroxine. The study included individuals with subclinical hypothyroidism. The patients were selected from outpatient /indoor department of the institution during the study period after fulfilling the inclusion and exclusion criteria.

Inclusion Criteria of the study

- a) Newly detected cases of hypothyroidism including subclinical hypothyroidism (with euthyroid individuals as controls).
- b) Age at least 18 years.
- c) Both males and females.
- d) No history of thyroxine in last three months.

Exclusion criteria

- a) Person on thyroxine treatment
- b) Pregnancy, lactating mothers, Renal disease, Liver disease, Cardiovascular disease, Hypertension, Diabetes Mellitus, Gout, Muscular disorders, Malignancy, Smoking, Alcoholism,
- c) Patients on drugs (Hypolipidemic drugs, Antihypertensives, steroids, probenacid, allopurinol, etc.).
- d) H/o chemotherapy or radiotherapy for malignancy was excluded.

The experimental protocol included:

1. Recording of detailed history including history of cardiovascular disease, diabetes mellitus, hypertension, surgery, or any drug intake and family history of renal, muscular, liver disorders.
2. Measurement of anthropometric indices like weight, height, BMI.
3. Recording of vital signs.
4. Blood investigations including serum uric acid, serum creatinine, fT3, fT4 and TSH.

Case selection

The data was collected by a preformed structured interviewer-administered questionnaire that was pretested with modifications made prior to its use in the study. The patients were

interviewed that requests for the history of cardiovascular disease, diabetes mellitus, hypertension, surgery, or any drug intake and family history of renal, muscular, liver disorders.

During the clinical visit, the information about demographics and a detailed medical history were obtained from the patients. Height was measured in centimeters and weight in kilograms by a calibrated scale with the subjects not wearing their shoes. The BMI was calculated as weight (in kilograms)/height² (in meters).

Collection of blood samples: About 2 ml of blood sample was collected in a yellow vacutainer, devoid of any anticoagulant and contained clotting agent to hasten the process of clotting. Blood samples after overnight fasting were collected from cases as well as controls. The samples were centrifuged and the serum was separated at the earliest. The serum was used for the estimation of serum T₃, T₄, TSH, creatinine and total creatine kinase activity.

Statistical analysis: Data so collected was tabulated in an excel sheet, under the guidance of statistician. The means and standard deviations of the measurements per group were used for statistical analysis (SPSS 22.00 for windows; SPSS inc, Chicago, USA). Difference between two groups was determined using student t-test as well as chi square test and the level of significance was set at $p < 0.05$.

Results

In both the groups, females were comparatively more as compared to males. 70% and 30% of the subjects in this study were female and male respectively. Maximum subjects were in the age group of 41-50 years (64% in case group, 56% in control group) followed by 31-40 years (22% in case group, 24% in control group). Mean age among the case and control groups was 42.14 ± 10.71 and 44.67 ± 12.32 respectively.

Mean BMI (kg/m^2) among the case and control group was 24.41 ± 0.89 and 22.08 ± 3.42 respectively. When mean BMI was compared statistically among case and control group, it was found to be statistically insignificant as $p > 0.05$.

Table 1: Thyroid profile among the study groups

Parameters	Case (Hypothyroid)		Control		t test	p value
	Mean	SD	Mean	SD		
T3 (ng/ml)	0.76	0.19	1.19	0.17	3.92	0.02*
T4 (ug/dl)	4.81	1.87	8.67	1.69	8.19	<0.01*
TSH (uIU/ml)	27.18	5.89	2.33	0.24	18.72	<0.01*

*: statistically significant

T3 (ng/ml) and T4 (ug/dl) was comparatively lower in case group (0.76 and 4.81 respectively) as compared to control group (1.19 and 8.67 respectively). TSH (uIU/ml) level was among the case and control group was 27.18 ± 5.89 and 2.33 ± 0.24 respectively. When mean T3 (ng/ml), T4 (ug/dl) and TSH (uIU/ml) was compared statistically among case and control group, it was found to be statistically significant as $p < 0.05$ (table 1).

Table 2: Comparison of mean Creatinine (mg/dl) & Uric Acid among the study groups

	Case (Hypothyroid)	Control	t test	p value
Creatinine				
Mean	1.39	0.93	3.07	0.04*
SD	0.18	0.24		
Uric Acid				
Mean	7.41	3.81	10.38	<0.01*
SD	2.37	1.84		

*: statistically significant

Mean creatinine (mg/dl) level was among the case and control group was 1.39 ± 0.18 and 0.93 ± 0.24 respectively. When mean creatinine (mg/dl) was compared statistically among case and control group, it was found to be statistically significant as $p < 0.05$. Mean uric acid (mg/dl) level was among the case and control group was 7.41 ± 2.37 and 3.81 ± 1.84 respectively. When mean uric acid (mg/dl) was compared statistically among case and control group, it was found to be statistically significant as $p < 0.05$. (Table 2)

Table 3: Correlation between thyroid profile and creatinine & Uric Acid

Parameters	r value	p value
T3 and Creatinine	-0.37	0.02*
T4 and Creatinine	-0.49	0.005*
TSH and Creatinine	0.54	<0.01*
T3 and Uric Acid	-0.42	0.009*
T4 and Uric Acid	-0.50	0.005*
TSH and Uric Acid	0.61	<0.01*

*: statistically significant

Pearson correlation test was applied to correlate thyroid profile with creatinine & Uric Acid. Negative significant correlation was found between T3 and creatinine ($r = -0.37$, $p = 0.02$) as well T4 and creatinine ($r = -0.49$, $p = 0.005$). Positive significant correlation was found between TSH and creatinine ($r = 0.54$, $p < 0.01$). Negative significant correlation was found between T3 and uric acid ($r = -0.42$, $p = 0.009$) as well T4 and creatinine ($r = -0.50$, $p = 0.005$). Positive significant correlation was found between TSH and uric acid ($r = 0.61$, $p < 0.01$) as shown in table 3.

Table 4: Comparison of Thyroid profile, creatinine & Uric Acid after treatment among the case group

Parameters	Pretreatment		Post-treatment		t test	p value
	Mean	SD	Mean	SD		
T3 (ng/ml)	0.76	0.19	0.91	0.28	3.14	0.002*
T4 (ug/dl)	4.81	1.87	5.98	1.86	3.02	0.03*
TSH (uIU/ml)	27.18	5.89	19.73	4.79	6.91	0.007*
Creatinine (mg/dl)	1.39	0.18	1.16	0.34	4.23	0.001*
Uric Acid (mg/dl)	7.41	2.37	5.18	2.09	4.99	0.001*

*: statistically significant

Table 4 shows the comparison of Thyroid profile after treatment among the case group. Post treatment there is improvement in all the thyroid parameters. The comparison of creatinine (mg/dl) and uric acid (mg/dl) after treatment among the case group. Post treatment there is reduction in creatinine (mg/dl) and uric acid (mg/dl) level, it was found to be statistically significant as $p < 0.05$.

Discussion

The clinical condition arising due to deficiency of thyroid hormones or fall in the thyroid hormones below the physiologic reference range is known as hypothyroidism. It further results in generalized fall in the metabolic processes of the body. It is well established fact that renal system is affected by hypothyroid states of the body⁵⁻⁶. Hence; we evaluated the effect of hypothyroidism on the renal functions of the body.

In both the groups, females were comparatively more as compared to males. 70% and 30% of the subjects in this study were female and male respectively. **Mamatha BV et al,**

2016⁷&Meenakshi, et al, 2016⁸ in their study found similar female dominancy which is similar to our study.

Mean age among the case and control groups was 42.14±10.71 and 44.67±12.32 respectively with statistically insignificant difference as $p>0.05$. In a study by Mamatha BV et al, 2016⁷, age of participants ranged between 20 and 59 years-old with mean age of 41 years which is approximately similar to our study.

T3 (ng/ml) and T4 (ug/dl) was comparatively lower in case group (0.76 and 4.81 respectively) as compared to control group (1.19 and 8.67 respectively). TSH (uIU/ml) level was among the case and control group was 27.18±5.89 and 2.33±0.24 respectively. When mean T3 (ng/ml), T4 (ug/dl) and TSH (uIU/ml) was compared statistically among case and control group, it was found to be statistically significant as $p<0.05$. Results were similar to study done by Meenakshi, et al⁸, 2016, Mamatha BV et al⁷, 2016&Jia et al⁹, 2015 in their study found that mean level of T3 in the control group and in the hypothyroid group was 1.15 and 0.82 ng/ml respectively. Mean level of T4 in the control group and hypothyroid group were 8.91 and 4.75 µg/dl respectively. While comparing the mean levels of T3, T4 and TSH in between the two study groups, significant difference was obtained.

In our study; mean creatinine (mg/dl) level was among the case and control group was 1.39±0.18 and 0.93±0.24 respectively. When mean creatinine (mg/dl) was compared statistically among case and control group, it was found to be statistically significant as $p<0.05$. The increase in serum creatinine may be either due to increased production or decreased renal clearance. Decreased glomerular filtration rate (GFR) is believed to be due to the generalized hypodynamic circulation in hypothyroid patients¹. Elevated creatinine levels in the present study is in accordance with study done by Ajaykumar N et al¹⁰, 2013, Mamatha BV et al⁷, 2016&Khan AH⁵, 2013.

In this study; mean uric acid (mg/dl) level was among the case and control group was 7.41±2.37 and 3.81±1.84 respectively with statistically significant difference as $p<0.05$ in this study. Khan AH⁵, 2013 in their study revealed that mean serum uric acid level in hypothyroid subjects was significantly higher than in control subjects. This finding is consistent with our study.

Pearson correlation test was applied to correlate thyroid profile and creatinine. Negative significant correlation was found between T3 and creatinine ($r=-0.37$, $p=0.02$) as well T4 and creatinine ($r=-0.49$, $p=0.005$). Positive significant correlation was found between TSH and creatinine ($r=0.54$, $p=<0.01$) in our study. Similarly, Mamatha BV et al⁷, 2016&Lyu X et al¹¹, 2015 in their study got significant positive correlation of TSH with serum creatinine.

In our study, Pearson correlation test was applied to correlate thyroid profile and uric acid. Negative significant correlation was found between T3 and uric acid ($r=-0.42$, $p=0.009$) as well T4 and creatinine ($r=-0.50$, $p=0.005$). Positive significant correlation was found between TSH and uric acid ($r=0.61$, $p=<0.01$). Similar correlation was reported by Mamatha BV et al⁷, 2016 and Khan AH⁵, 2013 in their study.

From the results of our study, patients presenting with these biochemical abnormalities are recommended to be investigated to explore hypothyroidism. As our sample size was small and duration of study was limited, further studies with larger sample size and longer duration are also recommended.

Conclusion

This study confirms that hypothyroidism is associated with a consistent elevation in the serum creatinine and uric acid levels. Therefore, we would suggest assessment of thyroid function in patients presenting with deranged renal function and also hypothyroidism should be taken into account, in patients presenting with the biochemical abnormalities of chronic kidney diseases.

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