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The Impact of Thyroid Hormone Therapy on the Changes in Estimated Glomerular Filtration Rate in Chronic Kidney Disease Patients with Subclinical Hypothyroidism

Kannan Rajalingam[1], Kandan Muralidharan[2],Victor Theophilus Premkumar [3]
[1]*Junior Resident, Department of Internal Medicine, Madurai Medical College.*
[2]*Assistant Professor, Department of Internal Medicine, Madurai Medical College.*
[3]*Former Professor & HOD, Department of Internal Medicine, Madurai Medical College.*
Corresponding Author:Dr. KandanMuralidharan

ABSTRACT
CONTEXT: *Thyroid hormones has a significant impact on kidney disease so it is important to consider the physiologicalassociation of thyroid dysfunction in relation to chronic kidney disease.Hypothyroidism is known to be associated with reduced renal plasma flow (RPF) and low glomerular filtration rate (GFR). Also it causes decreased renal sodium reabsorption and decreased renal ability to dilute urine, resulting in hyponatremia.*
SETTINGS AND DESIGN
Prospective study
MATERIALS AND METHODS
STUDYPOPULATION:
50 ultrasound defined non diabetic chronic kidney disease patients attending outpatient and inpatient department in GRH, Madurai.
INCLUSIONCRITERIA :
- *All non diabetic chronic kidney disease patients with subclinical hypothyroidism.*
- *Age group of 18 to 65.*

EXCLUSIONCRITERIA:
- *Hypothyroid patients already on treatment*
- *Diabetic patients*
- *Patients on concurrent treatment with lithium, amiodarone or iodine*

PERIODOFSTUDY:
6 Months
STATISTICAL ANALYSIS
Categorical data expressed in percentage and percentile.
Continuous data, mean, standard deviation calculated by ANOVA test.
RESULTS: *In this study total participants 50,in this 60% are males remaining 40% are females. Most of the person fall in 40 to 50 years of age.The mean value of TSH at baseline, end of third and sixth month respectively 7.28, 6.47 and 6.06, with significant P value of <0.001. The mean value of urea at baseline, end of third and sixth month respectively 74.72, 67.34 and 62.20, withsignificant P value of <0.001. The mean value of creatinine at baseline, end of third and sixth month respectively 2.33, 2.03 and 1.92, with significant P value of <0.001.The mean value of eGFR at baseline, end of third and sixth month respectively 32.16 , 37.97 and 40.21, with significant P value of <0.001*
CONCLUSIONS: *Thyroid hormone replacement for subclinical hypothyroidism may improve estimated glomerular filtration rate in chronic kidney disease patients. Thyroid hormone therapy may preserve renal function better in chronic kidney disease patients with subclinical hypothyroidism.*

KEYWORDS
eGFR - estimated Glomerular Filtration Rate
CKD - Chronic Kidney Disease
MDRD - Modification of Diet in Renal Disease

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I. Introduction:

Thyroid hormones has a significant impact on kidneydisease so it is important to consider the physiological association of thyroid dysfunction in relation to chronic kidney disease.Hypothyroidism is known to be associated with reduced renal plasma flow (RPF) and low glomerular filtration rate (GFR). Also it causes decreased renal sodium reabsorption and decreased renal ability to dilute urine, resulting in hyponatremia.Serum TSH concentrations are usually normal or elevated in Chronic Kidney Disease, but its response to its releasing hormone (TRH) is generally low.

These findings suggest the presence of intrathyroidal and pituitary disturbances associated with uremia. TSH glycosylation are altered in CKD. It may compromise TSH bioactivity.Elevated TSH and absence of rT3 rising differing from other nonthyroidal illness.

II. Materials And Methods:

Study Population:

The study will be conducted on 50 consecutive adult (age≥18 years) CKD patients attending outpatient and inpatient department of Government Rajaji Hospital & Madurai Medical College during the study period of 6 months.

Inclusion Criteria:

Non diabetic chronic kidney disease patients of various etiology as diagnosed by biochemical and radiological investigations.

Exclusion Criteria:

Hypothyroid patients already on treatment
Diabetic patients
Patients on concurrent treatment with lithium, amiodarone or iodine.

Ethical Committee Approval: Obtained.

Study Protocol:

50 CKD patient with specified norms was taken for the study. Initial values of serum TSH, T3,T4, blood urea, serum creatinine were measured. Patients treated with tablet Levothyroxine 25/50 microgram/day. Patients laboratory vales were repeated. Levothyroxine dose were titrated to maintain the serum TSH value should be kept in lower half of normal range. After 3 months all values were repeated and all the collected data were processed. Final results were supported the study's objective.

III. Statistical Analysis:

All data were entered in Excel 2007 and statistical analysis was performed using the statistical software SPSS 16.0.Data were expressed as frequency (with percentages), median values (with range (min, max)). For continuous variables, Mann Whitney U-test was performed to find the differences between two groups and for categorical variables Pearson's chi-square test was performed.Results were defined as statistically significant when the *P* value (2-sided) was less than 0.05.

IV. Results:

Baseline values of the patients

S.NO	PARAMETER	RANGE	MEAN
1	Age(years)	18 to 70	48
2	Fasting blood sugar(mg/dl)	70to 100	84
3	Postprandial blood sugar(mg/dl)	100to 140	132
4	Blood urea(mg/dl)	24to 423	224
5	Sr.creatinine(mg/dl)	1.8to 24.2	12.8
6	eGFR (ml/min/1.73m²)	16 to 71	32.16
7	Sr.uric acid(mg/dl)	3 to 7	5

8	TSH(µg/ml)	5.5to 9.8	8.1
9	Free T4(ng/dl)	0.4to 5.3	2.8
10	Free T3(pg/dl)	0.8to 4.2	3.4
11	ANA	Negative	
12	Urine albumin	+ to +++	++
13	Urine sugar	Nil	

Mean TSH with comparison

S.NO	DURATION	MEAN	S.D.	SIGNIFICANCE
1	BASELINE	7.28	1.06	<.001
2	3rd MONTH	6.47	1.01	<.001
3	6th MONTH	6.06	0.94	<.001

Mean creatinine with comparison

S.NO	DURATION	MEAN	S.D.	SIGNIFICANCE
1	BASELINE	2.33	0.71	<.001
2	3rd MONTH	2.03	0.61	<.001
3	6th MONTH	1.92	0.59	<.001

Mean eGFR with comparison

S.NO.	DURATION	MEAN	S.D.	SIGNIFICANCE
1	BASELINE	32.16	10.75	<.001
2	3rd MONTH	37.97	12.84	<.001
3	6th MONTH	40.21	13.30	<.001

V. Discussion:

Even though previous studies have demonstrated that restoration of euthyroidism has beneficial effects on cardiac dysfunction in patients with SCH, the impact of THRT on renal function has not been extensively explored in these patients. The results of this study show that thyroid hormone treatment significantly abrogated the decrease in eGFR in CKD patients with SCH. The data of 14,623 adult participants from the third National Health and Nutrition Examination Survey, a nationally representative sample of the United States population, revealed that the prevalence of hypothyroidism increased with lower levels of GFR, occurring in 10.9% of patients with stage 2 CKD, 21.0% with stage 3 CKD, and 23.1% with stage 4 or 5 CKD. Moreover, Chonchol M et al. showed that the prevalence of SCH increased from 7% at an eGFR 90 mL/min/1.73 m2 to 17.9% at an eGFR <60 mL/min/1.73 m2 in 3,089 unselected outpatient adults. Similarly in our study, the prevalence of hypothyroidism increased with declining levels of eGFR occurring in 3.1% of cases with stage 3b CKD, 25% cases with stage 4, and 71.9% of cases with stage 5 or end-stage renal disease. The incidence of hypothyroidism is up to 4/1000 women and 1/1000 men and the prevalence of OH increases with age. SCH is found in 6–8% of women (10% over the age of 60yrs) and 3% of men. This clearly demonstrates the higher prevalence of hypothyroidism in patients with chronic renal dysfunction. The effect of thyroid hormone replacement on renal function has not been widely investigated in hypothyroid CKD patients, especially in SCH. A recent study by Shin et al. demonstrated that thyroid hormone treatment not only preserved renal function but was also an independent predictor of renal outcome. However, they compared changes in eGFR in two different study populations. Thus, to clarify the direct impact of thyroid hormone treatment on the decline in renal function, it was imperative to compare decline in eGFR before and after L-thyroxine replacement in the same patient. The results of this study showed that THRT significantly improved the renal function as evidenced by mean eGFR (ml/min/1.73 m2) which increased from 32.16 ± 10.75to 37.97 ± 12.84 and 40.21 ± 13.30 after 3 and 6 months of THRT, respectively ($P < 0.001$).

VI. Conclusion:

Thyroid hormone replacement for subclinical hypothyroidism may improve estimated glomerular filtration rate in chronic kidney disease patients. Thyroid hormone therapy may preserve renal function better in chronic kidney disease patients with subclinical hypothyroidism.

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