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Research Article

Estimation of Thyroid Function Tests in Patients with Chronic Kidney Disease: A Cross Sectional Observational Study

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Abstract

Introduction: Abnormal thyroid functions tests are frequently observed in patients of chronic kidney disease (CKD). Kidneys play a significant role in thyroid hormone metabolism by converting T4 to T3 (the active metabolite). Low plasma T3 in end stage renal disease is a marker of inflammation and endothelial dysfunction and also a known cause for mortality.

Objectives: The study was undertaken to assess the biochemical abnormalities of thyroid function tests in CKD patients and to correlate the severity of CKD with thyroid function tests.

Methodology: A total of 45 (n=45) CKD patients attending outpatient or inpatient departments of general medicine and nephrology were included in this study. Informed consent was obtained from all the patients. All the biochemical reports of the patients viz. blood urea, serum creatinine, thyroid profile (TSH, TT3, TT4) were collected from the patients and values were entered in the individual patient case report form. Patient's symptoms with respect to renal and thyroid abnormality were also noted in the forms. Correlation between thyroid abnormalities and CKD stage were analyzed using Chi square test and ANOVA tests.

Results: The mean age of the CKD patients was 51.4 ± 12.6 years of which 35 were male and 10 were females. The mean value of TT3 in CKD stage III, IV and V were 112.5 ±15.8; 98.8±24.9; and 77.9±29 ng/ml, respectively (p= 0.02 significant). The mean value of TT4 in CKD stage III, IV and V were 6.47± 0.67; 5.12±1.16; 4.41±1.52 µg/ml, respectively (p=0.003 significant).

Conclusion: Total T3 and T4 were found to be progressively decreased as stage of CKD advances. There was a significant correlation between the prevalence of thyroid dysfunction and the stage of chronic kidney disease. Higher the degree of renal insuffiency, the greater was the prevalence of thyroid hormone abnormalities. The thyroid hormones i.e. T3, T4 level decreases and the TSH increases as the severity of renal failure advances. Thyroid hormone abnormalities could represent a risk factor for cardiovascular disease and might also be implicated in kidney disease progression.

Keywords: Chronic kidney disease, Hypothyroidism, Thyroid function test

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Introduction

"The major problem in the worldwide is global outbreak of chronic kidney disease (CKD). Even though the morbidity and mortality from infectious diseases is declining, but chronic degenerative diseases are becoming more prevalent. CKD is one of the most common among the chronic non-infectious illnesses".[1]

India being the largest reservoir of diabetic patients, diabetic nephropathy is the commonest cause of chronic kidney diseases in this country. There are about 7.85 million CKD patients in India.

Patients with chronic kidney disease exhibit a variety of endocrine disturbances. But, the evidence of endocrine dysfunction exists only in laboratory parameters; many of the patients are not associated with apparent clinical signs and symptoms of the disease.[2] CKD is a well known cause of non thyroidal illness causing thyroid dysfunction, i.e., alteration in thyroid parameters in the absence of underlying thyroid disease.[3]

Chronic kidney disease affects thyroid functions in multiple ways, decreasing circulating thyroid hormone concentration, interference in peripheral hormone metabolism, alteration in the binding of plasma proteins, reduction in tissue thyroid content and increased iodine stores in thyroid glands. Total T_3 (TT3) and total T_4 (TT4) are decreased more commonly in patients with chronic kidney disease. But there are normal TSH levels in these patients, indicating euthyroid status. It could be a natural defense mechanism of the body against protein wasting which might worsen protein malnutrition in chronic kidney disease.[4]

Previous studies have shown increased incidence of subclinical hypothyroidism in CKD patients and higher prevalence of hypothyroidism in patients with terminal renal failure. It was estimated that primary hypothyroidism may occur in up to 9.5% of end stage renal disease patients when compared to 0.6-1.1% of general population.[5]

Prolonged hypothyroidism if becomes severe it can cause reduced cardiac function and lead to further worsening kidney functions. Hence, the prevalence of thyroid dysfunction in patients with CKD might be a risk factor for both cardiovascular disease and kidney diseases.[6]

It has been found that in patients with kidney failure and pilot trials of T3 supplementation in other nonthyroidal illnesses may have a favorable influence on clinical outcomes in dialysis patients with low T3. [7]

In renal parenchymal disease, there are continuous insults to the nephron and causing adaptive hyper filtration in remaining nephrons. This adaptive hyper filtration results in long term glomerular damage causing to proteinuria and progressive deterioration of renal functions. Prolonged proteinuria causes a loss of thyroxine-binding globulin (TBG), transthyretin or prealbumin, and albumin leading to reduction in serum T4 and total T3 levels.[8] The present study was carried to assess the thyroid dysfunction in chronic kidney disease patients.

Methodology

This cross sectional observational study was carried out in Bapuji and Chigateri Hospitals attached to JJM Medical College, Davangere, Karnataka, India from November 2012 to September 2013. Ethical approval was obtained from the Institutional ethics committee prior to the study. A total of 45 (n=45) CKD patients, meeting inclusion criteria, attending outpatient or inpatient departments of general medicine and nephrology were included in this study. Informed consent was obtained from all the patients. Various biochemical reports of the patients' viz. blood urea, serum creatinine, thyroid profile were collected from all the patients and recorded in case report form. Patients symptoms were with respect to renal and thyroid abnormality were also noted in the forms.

Inclusion Criteria

- Symptoms of uremia >3 months
- Ultrasound evidence of chronic renal failure
- Supportive laboratory evidence of CKD like anemia, urine specific gravity changes in serum electrolytes, etc.

Exclusion Criteria

- Patients with CKD less than 18 years of age.
- Patients who have been diagnosed to be having thyroid disorder.
- Patients on drugs altering thyroid profile like amiodarone, steroids, dopamine, phenytoin, estrogen pills, and iodine containing drugs.
- Patients on thyroid hormone replacement or on antithyroid drugs.

Kidney function was assessed by estimated creatinine clearance which was calculated by using the cockcroft-gault equation.[9]

$$\text{Estimated Creatinine Clearance (ml/mt)} = \frac{(140 - \text{Age}) \text{ X } \text{Body weight in kg X } 0.85 \text{ (if female)}}{72 \text{ X Serum creatinine (mg/dl)}}$$

Stages of Chronic Kidney Disease (CKD)

The patients were classified into various CKD stages depending on their calculated GFR.[10]

Table 1.Stages of Chronic Kidney Disease (CKD)

Stage	GFR (ml/min) per 1.73m^2
0	>90[a]
1	≥90[b]
2	60-89
3	30-59
4	15-29
5	<15

Thyroid function was assessed by measuring serum TT3, TT4, and TSH by competitive chemiluminescent immuno assay and ultra sensitive sandwich chemiluminescent immuno assay (CLIA). Blood urea estimation was done by using diacetyl monoxime (DAM) method and serum creatinine by modified kinetic Jaffe method. All the biochemical tests were done in the central laboratory, JJM Medical College, Davangere, Karnataka, India. The following reference values were considered in the laboratory for thyroid parameters for the present study.

Normal values[11]

T3: 60-201.8ng/dl
T4: Males: 4.6-10.5µg/dl
Females: 5.13-14.06µg/dl
TSH: 0.27-4.2mIU/L

Statistical Analysis

All the information collected from the patients was entered in the master chart. Data analysis was done with the help of SPSS 15.0 software. Kruskal Wallis test was used to test the significance of difference between quantitative variable. One way ANOVA test was used to analyze various parameters like TT3, TT4, Blood urea and serum creatinine in relation to various grades of chronic kidney disease.

Results

In this study, we evaluated 45 patients with various grades of chronic kidney disease. Among 45 patients in the study sample, 35 patients were males, and remaining 10 patients were females. The age range was from 21 to 69 years. Most of the patients were in the age group of 51-60 years. And mean age was 51.2 years. Of the 45 CKD patients, 58% were diabetic, and 42% were hypertensive. Symptoms of hypothyroidism like tiredness, somnolence, weight gain, cold intolerance, constipation, hoarseness of voice etc., were noted in the study. Of the 45 CRF patients, only 9 patients (20%) were symptomatic and remaining 80% patients were asymptomatic (Table 2).

Among 45 CKD patients, 7 patients (14%) belonged to stage III, and 10 patients (20%) to stage IV and 28 patients (66%) to stage V of CKD (Table 3). We assessed the relationship between CKD stage and thyroid dysfunction by comparing thyroid profile and renal function test values. 28 patients in the stage 5 CKD had 10.71% hypothyroidism when compared to stage III (0%) and stage IV CKD (0%). And 17.85% of patients of stage V CKD had subclinical hypothyroidism when compared to stage III (0%) and stage IV CKD (10%). Some other hormonal abnormalities like decrease in TT3, TT4 and TSH, seen in stage IV and V CKD in a percentage of 50% and 42.85% respectively. So, higher the stage of CKD, greater was the prevalence of thyroid dysfunction. This correlation was found to be statistically significant (Table 4).

The mean blood urea of 73.7±8.4, 93.2±12.1, and 130.2±28.6 mg/dl were noted in stage III, IV and V CKD patients respectively. Similarly, serum creatinine was estimated to be 2.86±0.49; 3.48±0.49; 3.48±0.37; 7.55±2.09mg/dl in stage III, IV and V CKD patients respectively. Blood urea and serum creatinine levels were increased as stage of CKD advances and co-related to severity of hypothyroidism (Table 5).

The mean value TT3 were 112.5±15.8; 98.8±24.9; 77.9±29.5ng/dl respectively obtained in CKD stages III, IV and V. According to this study, we observed that as CKD stage advances, there was progressive decrease in TT3 levels which statistical significant ($p<0.05$). The mean values of TT4 were 6.47±0.67; 5.12±1.16; 4.41±1.52µg/dl respectively recorded in CKD stages III, IV and V. There was progressive decrease in TT4 as renal dysfunction advances with $p<0.05$. The mean TSH levels of 2.07±0.40, 3.68±2.31, 6.29±5.17 respectively observed in patients of CKD stages III, IV and V. The TSH level increased as stage of CKD advances and correlation was statistically significant.

Table 2.Prevalence of Symptoms of Hypothyroidism in CKD Patients

Symptoms	Cases	Percentage
Yes	09	20
No	36	80
Total	45	100

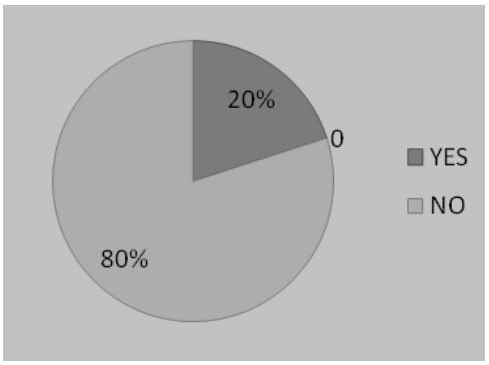

Figure 1.Pie Diagram Showing Prevalence of Symptoms of Hypothyroidism in CKD Patients

Table 3.The Prevalence of Patients in Various CKD Stages

CKD Stage	Number	Percentage
III	07	14
IV	10	20
V	28	66
Total	45	100

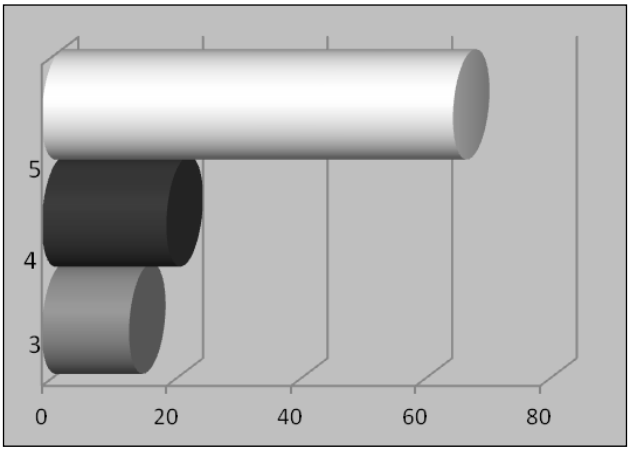

Figure 2.Bar Diagram Showing the Prevalence of Patients in Various CKD Stages

Table 4.The Relationships between CKD Stage and Thyroid Dysfunction

Thyroid Disorder	CKD stage					
	Stage III		Stage IV		Stage V	
	No	%	No	%	No	%
Hypothyroidism					03	10.71
Subclinical Hypothyroidism			01	10	05	17.85
Other thyroid hormonal dysfunction			05	50	12	42.85
Euthyroid state	07	100	04	40	8	28.59
Total	07	100	10	100	28	100
Chi square value	14.3	Statistically significant				
P value	0.0225					

Table 5.The Relationship between CKD Stage and Biochemical Parameters and their Significance

Parameters (mean±SD)	CKD stage			Statistical values	
	III	IV	V	F	P value
Blood urea	73.7±8.4	93.2±12.2	130.2±28.6	20.5	<0.001**
Serum creatinine	2.86±0.49	3.48±0.37	7.55±2.09	34.9	<0.001**
TT3	112.5±15.8	98.8±29.4	77.9±29.5	4.5	0.02*
TT4	6.47±0.67	5.12±1.16	4.41±1.52	6.69	0.003*
TSH	2.07±0.4	3.68±2.31	6.29±5.17	3.39	0.04*

F* = one way ANOVA test; **p value = <0.001 highly significant (HS); *p value <0.05 significant (S)

Discussion

Thyroid hormones play an important role in metabolism, development and influencing other hormonal functions. The two main hormones produced by the thyroid are triiodothyronine (T3) and thyroxine (T4). Disorders in thyroid function have been seen to coexist with chronic kidney diseases.[12]

The kidney normally plays an important role in the metabolism, degradation, and excretion of several thyroid hormones. The impairment in kidney functions leads to disturbance in thyroid physiology. All levels of the hypothalamic- pituitary- thyroid axis may be involved, including alteration in hormone production, distribution, and excretion.

Patients with CKD often doesn't have signs and symptoms suggestive of thyroid dysfunction and hence the diagnosis of thyroid disease in these patients becomes difficult.. It has been found that the risk of death was 2.7 times higher in patients with persistently low T3 compared with those with persistently high levels, and the risk of cardiovascular death associated with persistently low T3 was even greater.[13]

Previous study by Meuwese et al concluded that low T3 is a marker of LV hypertrophy and cardiomyopathy and an independent death predictor in follow-up studies in dialysis patients.[14]

In this study most of the CKD patients were asymptomatic with subclinical hypothyroidism. This result coincides with the result of the previous study done by Mehtal HJ et al.[15]

The only limitation of this study was sample size. However, we are planning to extend this study in upcoming time.

Conclusion

Total T3 and T4 were found to be progressively decreased as stage of CKD advances. There was a significant correlation between the prevalence of thyroid dysfunction and the stage of chronic kidney disease. Higher the degree of renal insuffiency, the greater was the prevalence of thyroid hormone abnormalities. The thyroid hormones i.e. T3, T4 level decreases and the TSH increases as the severity of renal failure advances. Thyroid hormone abnormalities could represent a risk factor for cardiovascular disease and might also be implicated in kidney disease progression.

Conflict of Interest: None

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